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Medical Research

The Program of the U. S. Public Health Service

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▪ Federal Government expenditures for medical research have increased apace in the last ten years. The increase in federal research funds has stimulated support from private sources; contributions from other than federal sources have doubled.

More than half of medical research funds are being used by universities, hospitals, and other nonprofit institutions, and less than one-fourth by laboratories of the Federal Government.

Grants-in-aid of research, fellowships and extended training are made on the advice of Advisory Councils made up of leaders in the various research fields. The previous record of research by staffs and faculties of institutions is taken into account. Special attention is given to unknown investigators and small projects.

Noninterference with a scientist in the conduct of research is a basic principle of all grants. He may change the direction of his research to pursue promising leads without asking permission.

Continuity of grants so that promising projects need not be abandoned at the end of a grant period is given special consideration.

REMARKABLE CHANGES have taken place since World War II both in the substance of medical research in this country and in the sources of support for the total national medical research effort. Several penetrating analyses of the dynamic factors influencing these changes are readily available. It is not my purpose, however, to discuss the impact on present-day medical science of these complex factors such as the many-faceted wartime research and development program, and the rapidly converging interests of the physical, biological, and medical sciences. Rather, it is my purpose to consider briefly one significant alteration in the environment in which medical research is being conducted and to outline the role of the United States Public Health Service in encouraging and assisting medical research of high quality in universities, hospitals and other research institutions throughout the country.

Last year Dr. James A. Shannon, Director of the National Institutes of Health in Bethesda, Maryland, the research bureau of the Public Health Service, voiced the following opinion before the Clinical Sessions of the American Medical Association in Boston: "Viewed in perspective, the past decade has been the first period in our history when the national medical research effort was financed on a scale reasonably commensurate with the potential humanitarian and economic gain to be derived from such effort."[1] In this discussion of "Trends in Medical Research," Dr. Shannon drew attention to a significant recent phenomenon—namely, widespread public interest and public determination to support medical research. Such vital encouragement of medi-

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cal scientists has resulted both in the augmentation of total funds available from all private and public sources, and in increased appropriations of federal tax funds in support of medical research.

It is estimated that in 1947, the total national expenditure for medical research amounted to about $87.5 million, more than twice the amount available for these purposes in the immediate pre-war period. Of the 1947 expenditures, federal tax support amounted to $28 million, about 32 per cent of the total; in 1940, just before the war, the federal contribution to our national medical research program was about $3 million, about 7 per cent of the total. The best available figures for 1957 at the time of this writing indicated that some $330 million was to be spent for medical research, with roughly 56 per cent of that amount ($186 million) to be supplied by the Federal Government. Thus, in the last 11 years, total national medical research funds have increased almost fourfold; federal contributions in support of medical research have increased more than sixfold during the same period, and now represent more than half of the total.

It is highly significant that, during this same post-war period, support of medical research from other sources—from industry, from private philanthropy and from income from endowment—has not fallen, as some had feared, but in fact has doubled. This increase, however, has not been proportional to that of the federal share. In this regard it is worthy of emphasis that federal expenditures for medical research have stimulated and encouraged more substantial support from other sources. It may also be pertinent to point out that despite this substantial growth, today less than 5 per cent of the nation's total research and development effort is devoted to medical research.

Of equal importance to the sources of financial support of medical research are the channels through which these funds are expended. Although more than half of the national medical research funds are derived from federal appropriations and only about one-sixth from private sources other than industry (philanthropy, plus income from endowment), almost the reverse is true in terms of use. More than half of medical research funds are being used by universities, hospitals and other nonprofit institutions and less than one-quarter by research laboratories of the Federal Government. Industry contributes about one-fourth of the total and expends almost an equal proportion. Stated in slightly different terms, of the $255 million medical research program carried on in nonfederal laboratories and research institutions, $111 million, or almost 45 per cent of the cost of all private medical research, is being met with federal funds.

Five federal agencies—the Department of Defense, the Atomic Energy Commission, the Veterans Administration, the National Science Foundation and the Department of Health, Education, and Welfare—are each making a significant contribution to the nation's medical research effort. The roles assigned to each through legislative authorization merge one with the other, but there can be little doubt that these programs are complementary and in no sense compete either for federal funds or in the application of their resources to useful purposes.

At present the Department of Health, Education, and Welfare, and particularly its component health agency, the Public Health Service, occupies a dominant place in the support of medical research through the use of federal tax funds. In turn, the National Institutes of Health, the principal research arm of the Public Health Service, is charged with dual medical research responsibilities. One of these responsibilities is to conduct medical and related research within its own laboratories and facilities, including the Clinical Center at Bethesda, Maryland, and a number of field stations in various parts of the country. The other is to aid in the support of individual scientists or groups of scientists working in universities, hospitals, laboratories, and other public and private nonprofit institutions throughout the country. It may be of interest to note that more than two-thirds of National Institute of Health (NIH) funds are expended in our so-called extramural activities—grants and awards to non-federal scientists. Less than one-third is spent on intramural or direct operations. Although the NIH constitutes the primary focus of medical research activity within the Public Health Service, the other principal Bureaus of the Service—the Bureau of Medical Services and the Bureau of State Services—are also engaged in investigative and research activities. It is a fundamental belief of those who guide Public Health Service programs that an active research program is essential to the establishment and maintenance of highest standards of performance in all its assigned tasks.

The roots of the Public Health Service program of medical research can be traced back readily to 1887, when the service established one of the first bacteriology laboratories in this country. This was in response to the urgent need to guard against the introduction and transmission of epidemic disease by the large number of persons then flocking to these shores. Those familiar with the history of modern preventive medicine will recognize such names as Rosenau, Goldberger, Anderson, Frost, Lumsden and others that were identified with the Public Health Service Hygienic Laboratory, which in 1930 became the National Institutes of Health.

In 1937 Congress established the first of our present-day categorical institutes, the National Cancer Institute. Six additional categorical institutes were created in the post-war period 1948-1950: National Heart Institute, National Institute of Allergy and Infectious Diseases, National Institute of Arthritis and Metabolic Diseases, National Institute of Dental Research, National Institute of Mental Health, and National Institute of Neurological Diseases and Blindness. The Division of Research Grants, with administrative responsibility for the management and policy direction of the Public Health Service research grant program, was also established in the same period.

Each institute has been authorized by Congress to conduct research within its own facilities. In addition, each is authorized to support research into the causes, diagnosis, prevention and treatment of diseases and disabilities of man through grants and fellowships to nonfederal scientists. The institutes also support certain types of academic and research training.

Congress, in establishing these institutes, provided a very broad interpretation of each categorical area so that scientists seeking support of their research activities need not fear restrictive limitations on the project design or the direction in which their investigative efforts might lead. To fill any gaps that might lie outside the interests of one or more institutes, Congress has authorized the Division of Research Grants to make grants of a totally noncategorical nature.

More recently, additional research grant and award authority has been assigned to the Public Health Service. Today, not only the National Institutes of Health, but also the Division of Hospital and Medical Facilities and the Division of Nursing Resources in the Bureau of Medical Services, the Division of Sanitary Engineering Services, and the Division of Special Health Services in the Bureau of State Services are actively engaged in the Public Health Service research program.

By Congressional authority, nine National Advisory Councils have been established as advisors to the Public Health Service. No research or training grant may be made by the Surgeon General unless recommended for approval by one of these councils. Seven of the councils advise the seven institutes of the National Institutes of Health on their respective programs, in addition to reviewing and recommending appropriate action on applications for grant support. The National Advisory Health Council reviews applications for general or noncategorical research grants not falling within the interest of the institutes, and advises the Surgeon General on matters relating to general health activities and functions of the service. The Federal Hospital Council advises the Surgeon General on matters relating to the administration of the Hospital Survey and Constructions Program and reviews applications for grants-in-aid of projects relating to hospital services, facilities, and resources.

The National Advisory Council on Health Research Facilities, established in July 1956, reviews and recommends appropriate action on applications submitted by universities or other nonprofit institutions for assistance in the construction and/or equipping of additional facilities for the conduct of research in the sciences relating to health.

In view of the large number of applications submitted to the National Institutes of Health, covering the entire range of medical and biological research, the National Advisory Councils require the advice of many technical consultants. It was estimated that between 9,000 and 10,000 applications would be processed in 1957, of which some 6,000 would be supported through grants. The Division of Research Grants, therefore, has established over thirty study sections and other review committees. The members of these study sections and review committees are recognized leaders in the various fields of research, and, for the most part, are scientists in nonfederal agencies. In effect, then, these scientists, representing diverse fields and interests outside of government, act as technical advisors to the National Advisory Councils and to the Surgeon General. They accept responsibility not only for providing technical advice on applications for research support, but also, in conjunction with the councils, for surveying as scientific leaders the status of research in their particular fields in order to determine areas in which additional activity should be initiated or expanded.

Let me now outline briefly the principal types of grants and awards made by the Public Health Service in support of research, training, and construction:

1. *Research Grants.* Research grants are made to universities, hospitals, laboratories and other public or private institutions and to individuals for support of research projects in health, medicine and allied fields, including experiments or demonstrations relating to the development, utilization, and coordination of hospital services, facilities, and resources. The major objectives of the research grant program are (1) to expand medical and biological activities in research institutions throughout the country; (2) to provide on-the-job training for scientific personnel in connection with the research being conducted; and (3) to stimulate new investigations in fields needing exploration. These funds provide for salaries, equipment, supplies, travel and other expenses.

2. *Research Fellowships.* Research fellowships of five types are available: (a) *Predoctoral Research Fellowship,* awarded to qualified persons who hold a bachelor's degree or equivalent training. Fellows are expected to carry on studies oriented toward graduate training in fields related to the health sciences. (b) *Postdoctoral Research Fellowship,* awarded to qualified persons holding a doctor's degree in medicine, dentistry or related fields. Stipends and extra allowances are awarded under established Public Health Service policy. (c) *Special Research Fellowship,* awarded to qualified applicants who have demonstrated unusual competence for research, or who require specialized training for a specific problem. The amount of the stipend is set in each case. (d) *Student Part-time Research Fellowship,* designed to give students in medicine, dentistry, nursing and public health an opportunity to explore the research field in the hope that many of those supported will enter into full or part-time research careers. A predetermined number of these fellowships may be awarded each year. (e) *Senior Research Fellowship,* granted in support of preclinical science investigators between the completion of postdoctoral training and eligibility for permanent academic appointment. These funds provide for salaries plus research expenses not exceeding $2,000. The Senior Research Fellows may also apply for research grants to support their research.

3. *Undergraduate Training Grants.* Undergraduate training grants are awarded to medical schools, dental schools, public health schools and schools of nursing to assist in developing expanded and better integrated undergraduate instruction in the special fields concerned. It is the responsibility of the institution to determine the most appropriate use of the funds.

4. *Graduate Training Grants.* Graduate training grants are awarded to public and private nonprofit institutions interested in providing special training for researchers, teachers and prospective practitioners interested in public service. These funds may be used to improve facilities and to provide salaries for faculty, staff and trainees, along with necessary supplies and materials.

5. *Traineeships.* A series of traineeship stipends are awarded either directly to the individual in training or through a training grant to the institution for this purpose. Traineeships are awarded to physicians and other professional personnel in order to encourage specialization in one of the branches of medicine supported. Stipends and extra allowances are made under established PHS policy.

6. *Health Research Facilities.* Under the Health Research Facilities Act, July 1956, the Congress authorized the establishment of a program to assist in the construction and/or equipping of additional facilities for the conduct of research in the sciences relating to health by providing grants-in-aid on a matching basis to public and private nonprofit institutions. The amount of federal funds awarded may not exceed 50 per cent of the total costs of the research portion of the facility, the remaining sum to be provided from nonfederal sources.

Public Health Service programs in support of research and training in universities, hospitals and other nonfederal institutions have justified continued Congressional interest, as evidenced in the following table which shows the growth of the programs by appropriation year:

	Research Grants	Fellowships	Training Grants*	Health Research Facilities
1946	$ 780,000	$ 44,000	$ 29,000	$ .....
1947	3,576,000	178,000	250,000	.....
1948	9,145,000	520,000	2,810,000	2,303,000
1949	10,871,000	1,115,000	3,930,000	.....
1950	13,065,000	1,448,000	6,415,000	5,775,000
1951	16,713,000	1,565,000	6,928,000	9,459,000
1952	18,173,000	1,755,000	7,392,000	4,625,000
1953	20,374,000	2,024,000	8,194,000	.....
1954	28,866,000	2,133,000	10,813,000	.....
1955	33,918,000	2,562,000	11,051,000	.....
1956	38,038,000	2,800,000	14,502,000	.....
1957	93,300,000	5,397,000	28,075,000	30,000,000

*Includes traineeships.

May 8, 1957

Many other aspects of the Public Health Service research grant and award program could profitably be reviewed. Within the limitations of this presentation, however, it is necessary to select only a few additional principles that are basic to the operation of our total program. I shall refer to the need for safeguarding the scientific freedom of the investigator; the importance of continuity and stability of support; and to equitable distribution, geographic and otherwise, of research grants and awards.

Scientific Freedom of Investigator

Noninterference with the scientist in the conduct of his research is the most important principle underlying our program. A number of safeguards have been established to insure that the Public Health Service in no way controls the research carried out under the grants. These measures include: (1) The legislation itself, which vests in the National Advisory Councils the authority for selecting the applications meriting support; (2) the awarding of grants on the basis of competent review by the applicant's scientific peers; (3) permission to publish results without previous clearance from or notification to the Public Health Service; (4) freedom of the grantee, once a grant has been awarded, to make substantial transfers between budget categories without previous approval; (5) provision for the grantee institution to administer the grant under

the rules and regulations of that institution, rather than under Public Health Service rules; (6) vesting in the grantee institution of title to all equipment purchased with grant funds; and (7) authority to the scientist to change his research plans without need for getting approval if he finds new and more promising leads. These safeguards guarantee to the scientist that he will have the scientific freedom required for the best work.

Stability of Support

Stability of support for the investigator is also one of the chief concerns of those responsible for administering the research program of the Public Health Service. Readily conceding the preferability of endowment or other so-called "hard money," but recognizing the often frustrating and disappointing results of universities in obtaining such funds, the Public Health Service has developed policy to provide the maximum stability practicable under an annual appropriation project plan. An applicant who receives a grant for a year may also receive a moral commitment of from one to four additional years of support—a promise to pay, provided Congress appropriates the necessary funds. At the end of the committed period, the grantee often receives additional years of support after the National Advisory Councils and study sections have evaluated his needs and plans. Under this procedure a grantee may conceivably receive Public Health Service support of his research for an indefinite period.

Distribution of Research Grants and Awards

On several occasions studies have been made of the distribution of Public Health Service grant awards to institutions and to geographic areas of the country. As might be expected, the number of institutions sponsoring scientists receiving Public Health Service awards is quite large and increases with each passing year. It is of interest, however, that a relatively small number of institutions account for a large number of grants. For example, ten institutions received 35 per cent of all Public Health Service research grants in 1953. Using an index of research potential based on the percentage of faculty members listed in American Men of Science and the percentage of articles they have published in 53 leading periodicals, one finds a rather pronounced degree of correlation between grant awards and the research potential of an educational institution. The same is true when grants are analyzed geographically. Last year, for instance, the Pacific States (California, Oregon and Washington) received 12.8 per cent of the grants, whereas 11.7 of established scientists were located in this area. Since projects are evaluated primarily on the basis of merit, these findings were anticipated even though effort is made to help unknown investigators and institutions or agencies that have only small research programs. We believe these efforts are most important in the individual case even though they affect only slightly the over-all distribution of funds.

National Institutes of Health, Bethesda 14, Maryland.

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Congestive Heart Failure in Infants and Children

SAUL J. ROBINSON, *M.D.*, San Francisco

• **Congestive failure in infants and children is not uncommon and may be present in a varying number of conditions, particularly in certain types of congenital heart disease. Its recognition and proper treatment are usually followed by improvement, except in those instances where the failure is associated with a lesion incompatible with life. The essentials of treatment are: Treatment of the underlying cause, administration of a digitalis preparation, low salt diet, diuretics, rest and sedation, oxygen, adequate diet and, in rare instances, the use of steroids.**

CONGESTIVE HEART FAILURE occurs in as many as 10 to 20 per cent of all cases of heart disease in infants and children. The response to proper treatment of this condition is often dramatic and life saving.

Causes of Heart Failure

Most cases of heart failure in infants and children are due to congenital heart disease of one kind or another. In early infancy aortic atresia and transposition of the great vessels may give rise to failure, and treatment may be of only temporary benefit.[4] However, such curable lesions as patent ductus arteriosus, coarctation of the aorta and severe pulmonary stenosis may also be complicated by congestive failure which, if properly recognized and treated, may subsequently permit the surgical correction of the lesion. Combined lesions such as patent ductus arteriosus associated with an interventricular septal defect or with aortic stenosis are particularly likely to bring about heart failure in infancy.

In addition to congenital heart disease there are other conditions which may cause heart failure, among them pronounced anemia, hypothyroidism, sickle cell crisis, acute glomerulonephritis, paroxysmal atrial tachycardia,[2] thyrotoxicosis, diphtheria, "beri-beri heart," administration of desoxycorticosterone acetate or other steroids, rheumatic fever, cerebral vascular accident, subacute bacterial endocarditis, constrictive pericarditis, coronary artery occlusion, fibroelastosis and nonspecific myocarditis.

Clinical Features of Congestive Cardiac Failure

The clinical features of congestive failure are sometimes difficult to recognize in an infant or child and are often confused with those of infection. It is difficult if not impossible to differentiate between left heart and right heart failure in the young age group.[7] In general, signs of right heart failure predominate, and are:

1. *Rapid respirations.* The normal respiratory rate at birth and soon thereafter is approximately 40 per minute. It may range from 50 to 100 per minute and still not be identified as a sign of abnormality. Of course fever, particularly associated with a pulmonary infection, may produce rapid respirations. In cyanotic heart disease rapid respirations may be due to associated attacks of cerebral anoxia and not congestive failure; and the treatment for these two conditions is entirely different.

2. *Hepatomegaly.* The lower edge of the liver is easily palpated in infancy and can be one to two centimeters below the right costal margin without abnormality. The edge may be even lower in the presence of respiratory infection causing increased expansion of the lungs—as in bronchiolitis—in which case it is not enlarged but merely displaced caudally. Usually in such circumstances the spleen is more easily palpable. In true congestive failure, however, the liver is usually decidedly enlarged and the lower edge may be percussed or palpated at the umbilicus. Hepatomegaly not only is a sign of congestive failure, but a decrease in size is an excellent criterion of response to therapy.

3. *Cardiac enlargement.* Cardiac enlargement usually precedes and accompanies congestive heart failure.[9] In infants and children the size of the heart is difficult to determine radiologically, particularly if there is a superimposed thymic shadow. A greatly enlarged cardiac shadow unassociated with signs of congestive failure should lead to the suspicion that the shadow is not due to an enlarged heart.

4. *Tachycardia.* Although the rate is difficult to evaluate in a crying or moving child, a rate of 120 per minute or over in the absence of fever or crying, and when accompanied by rapid respirations and hepatomegaly, is indicative of tachycardia.

5. *Gallop rhythm.* A gallop rhythm usually denotes congestive failure, but this rhythm must be differentiated from the physiological third heart sound.

6. *Pulmonary rales.* Rales may be heard at both lung bases but are infrequent in infants, and when

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TABLE 1.—*Data on Administration, Action, Duration and Toxicity of Various Digitalis Preparations*

Agent	Method of Administration	Onset of Action	Time for Maximum Effect	Duration of Effect	Maximum Duration Toxicity
Digitalis leaf	Oral	6 hr.	12 to 48 hr.	17 days	1 to 2 weeks
Digitalis, injection USP	Intravenous or intramuscular	2 hr.	6 hr.	17 to 21 days	1 to 2 weeks
Gitalin	Oral	.....	24 to 48 hr.	10 to 12 days	.....
Digitoxin	Intravenous or intramuscular	30 min.	2 to 9 hr.	21 days	3 weeks
	Oral	2 hr.			
Digoxin (lanoxin)	Intravenous or intramuscular	30 min.	4 to 6 hr.	4 to 7 days	1 to 2 days
	Oral	2 hr.			
Lanatosid C or D (Cedilanid)	Intravenous or intramuscular	10 to 30 min.	2 to 3 hr.	2 to 3 days	1 day
	Oral	Absorption indefinite			
Ouabain	Intravenous	5 min.	30 min.	1 to 4 days	2 to 6 hr.
Acetyl strophanthidin	Intravenous	½ to 5 min.	12 min.	2 hours	30 min.

present are difficult to differentiate from those due to the pulmonary infection which frequently accompanies failure.

7. *Peripheral edema.* Edema is a very late sign of failure in infants and children. It indicates a very severe degree of failure.

8. *Easy fatigability.* This sign may be an important clue in detecting congestive failure in infants, and often it is the mother who notices that the infant pauses frequently to rest during his feedings.

The determination of venous pressure, vital capacity and circulation time is difficult in infants and small children, and are then only confirmatory procedures utilized after congestive failure has already been suspected by other signs and symptoms.

Treatment

Proper treatment of heart failure depends upon the application of certain fundamental measures, without, however, undue reliance on any one phase of treatment, and with close observation at all times. These fundamentals include:

1. *Treatment of the underlying condition.* Congestive failure is often precipitated by an infection or electrolyte imbalance, particularly in a child with a low reserve. Hence a child with pneumonia and heart failure should be vigorously treated with antibiotics, and one who has pronounced anemia should have careful replacement of blood. In conditions such as coarctation of the aorta, patent ductus arteriosus and severe pulmonary stenosis, surgical intervention must not be postponed too long, for operation may be the only way congestive failure may ultimately be relieved.

2. *Digitalis.* Use of a digitalis preparation is the basis of treatment for congestive failure.[6] There is nowadays no general reluctance to use such preparations in infants and children. One must not rely on it too much; although in most instances an average digitalizing dose will be effective,[1] the individual variability of response must be kept in mind. Whichever digitalis preparation is used, the therapist must be familiar with certain basic factors concerning it: The average digitalizing dose for the age and weight of the infant or child, the rapidity of action by both oral and parenteral routes, and the signs of toxicity. The most commonly used preparations are: Digitalis leaf or tincture, digitoxin, Digoxin® (lanoxin),[8] lanatosid C or D, acetyl digitoxin (Acylanid®) and Gitalin.®

Digitalis leaf acts slowly and dissipates slowly. Lanatosid C or D acts rapidly and is swiftly dissipated. The other preparations are between these extremes. Table 1 shows the method of administration, the onset of action, the time for maximal effect, duration of effect and the maximal duration of toxicity for each of the preparations mentioned. The usual method of administration and the digitalizing doses of these preparations are shown in Table 2. It is extremely important that one learn the vagaries of one or more preparations well, particularly with glycosides (the dose of which is 1/1000 that of a whole leaf preparation) for errors of dosage or in calculation of duration of effect may be disastrous.

It is difficult to determine how long to continue administration of digitalis once the congestive failure has been controlled. In general it may well be continued beyond the time the underlying cause has been eliminated. In prolonged administration of digitalis to an infant, the relatively rapid weight gain in this age group must be kept in mind, lest the patient outgrow the calculated dose.

One must not rely on digitalis alone, increasing doses to the point of toxicity before resorting to adjunctive therapeutic measures such as low salt diet and mercurial diuretics, or before investigating the reasons for ineffectiveness of the preparation. For

TABLE 2.—Dosage of Various Digitalis Preparations for Infants* and Children*

Agent	Method of Administration		Digitalizing Dose	Maintenance Dose
Digitalis leaf	Oral	Infant	15 mg./lb.	1/10 total digitalizing dose
		Child	10 mg./lb.	
		Adolescent or adult	1.2 to 2.0 gm. (average 1.5 gm.)	
Gitalin	Oral	Infant	0.02 to 0.04 mg./lb.	1/10 total digitalizing dose
		Child	0.01 to 0.02 mg./lb.	
		Adolescent or adult	3.0 to 10.5 mg. (average 5.7 mg.)	
Digitoxin	Oral, intravenous or intramuscular	Infant	0.02 to 0.03 mg./lb.	1/10 total digitalizing dose
		Child	0.01 to 0.02 mg./lb.	
		Adolescent or adult	1.3 to 2.0 mg. (average 1.7 mg.)	
Digoxin (lanoxin)	Intravenous or intramuscular	Infant	0.02 to 0.03 mg./lb.	
		Child	0.01 to 0.02 mg./lb.	
		Adolescent or adult	0.75 to 1.0 mg. (average 0.8 mg.)	1/10 to ¼ total digitalizing dose
	Oral	Infant	0.03 to 0.04 mg./lb.	
		Child	0.02 to 0.03 mg./lb.	
		Adolescent or adult	2.0 to 5.0 mg. (average 3.75 mg.)	
Lanatosid C or D	Intramuscular or intravenous	Infant	0.01 to 0.02 mg./lb.	1/10 to ¼ total digitalizing dose
		Child	0.008 to 0.01 mg./lb.	
		Adolescent or adult	1.2 to 3.2 mg. (average 1.6 mg.)	
Ouabain	Intravenous	Infant	0.006 to 0.008 mg./lb.	Not used
		Child	0.006 to 0.008 mg./lb.	
		Adolescent or adult	0.6 to 1.0 mg. (average 0.7 mg.)	

Safe average digitalizing dose for purified glycosides 0.015 mg./lb.

*Infant is under 2 years; child is 2 to 12 years.

example giving digitalis to a patient with hypokalemia may result in toxic arrhythmias without having any therapeutic effect until the potassium level is brought up to normal.[1,5] Sometimes when manifestations of digitalis toxicity develop, administration of potassium may relieve them even though the blood potassium content is already normal. It must also be kept in mind that since calcium and digitalis are synergistic, one must be cautious in using them simultaneously or consecutively.[3]

3. *Low salt diet.* A low salt diet is an invaluable adjunct in the treatment of congestive failure. In infants the administration of Lonolac,® a powdered milk, or the use of one of the recent low-salt evaporated or whole milk preparations which are now available in California should be instituted at the same time as the administration of the digitalis in any case of severe congestive failure. After the acute phase is over, it may be possible to permit the infant to have a modified or even regular salt intake without ill effect.

4. *Diuretics.* If digitalis and a low salt diet are not completely effective, use of a diuretic is indicated. There are several available preparations of both the mercurial and nonmercurial types. Thiomerin® (mercaptomerin sodium) has been used in pediatric cardiology because it can be given subcutaneously, and it is now very widely used in adult cardiology, as it seems to be somewhat safer than other preparations. The administration of 0.1 cc. of Thiomerin subcutaneously as a test dose can be followed by the administration of 0.12 to 0.25 cc. to an infant under one year, and 0.25 to 0.5 cc. to older children. It is usually best to give it every other day, and to discontinue it as soon as a response is obtained and maintained. Other diuretics such as Mercuhydrin® (meralluride sodium) may also be used. An oral preparation known as Diamox® (acetazoleamide), a carbonic anhydrase inhibitor, may be given in a dose of 2 to 3 mg. per pound of body weight per day. With the administration of mercurial diuretics, two precautions must be observed: (1) The loss of chlorides may produce alkalosis, which will make the mercurial diuretic ineffective until the loss is restored; (2) with pronounced diuresis a low salt syndrome may develop, with drowsiness and even stupor,[3] particularly in very warm climates. The rapid loss of fluid in diuresis may result in hypopotassemia, which may not only render the further administration of digitalis ineffective but result in digitalis intoxication.

5. *Rest and sedation.* Bed rest, and in some in-

stances the orthopneic position, are necessary. If drugs are necessary for complete rest, they should be given phenobarbital if it is adequate, and, if not, morphine sulfate in a dosage of 1 mg. per 10 pounds of body weight. Tranquilizers may merit consideration but they have not yet been used enough for this purpose to be recommended.

6. *Oxygen.* Oxygen administered in approximately 40 to 50 per cent concentrations seems to have a sedative effect in many cases, and also slows both the pulse and respirations. If pulmonary edema is present, oxygen should be bubbled through 50 per cent ethyl alcohol and given for five to ten minutes every hour or half-hour.

7. *Diet.* The diet should be essentially fluid in the early stages of treatment, after which a nutritious diet high in vitamin content should be used, with regulation of sodium content as needed.

8. *Cortisone.* Although steroids themselves may be a cause of congestive failure in rare instances, it has been reported that the use of cortisone or corticotropin (ACTH) may relieve severe cardiac failure due to rheumatic fever in some cases. They must be used with caution, however.

9. *Phlebotomy or venesection.* This measure is rarely used, but has been helpful in instances where overzealous administration of blood postoperatively has resulted in the precipitation or aggravation of heart failure.

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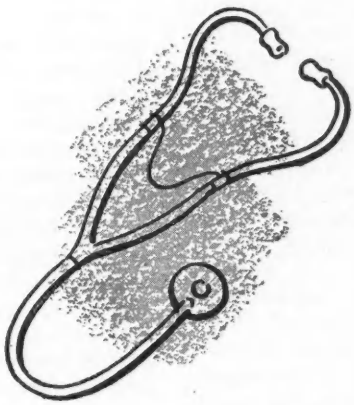

The Management of Cancer of the Breast

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• **Radical mastectomy is excellent only for cases of operable breast cancer in which the tumor is limited to the breast or to the nodes in the axilla. That there is metastasis to the internal mammary lymph nodes in a high proportion of cases has been "overlooked" for many years. Also it is probable that metastasis occurs to the supraclavicular lymph nodes more often than is suspected. Hence the extended radical mastectomy operation leaves much to be desired. There has been no significant improvement in recent years in the mortality rate of mammary cancer.**

Simple mastectomy and thorough adequate postoperative radiation therapy have much to offer.

Treatment of "operable" breast cancer should be a cooperative effort of surgeon, radiation therapist and pathologist.

CANCER OF THE BREAST is the most common malignant neoplasm occurring in women in this country. There has been no significant change in the death rates from breast cancer in California from 1920 to 1954.[12]

One factor in reported improvements in five-year survival rates is that since patients are now selected for operation with greater care than previously, operation is less often done in inoperable cases. Although use of surgical procedures in inoperable circumstances probably increase the rate of growth of the cancer and shortens life, in some such cases simple mastectomy may be indicated to remove a large ulcerated lesion as a palliative measure.

Perhaps the most widely accepted and universally employed operation in cancer therapy is radical mastectomy in the expectation of removing the primary cancer, its immediate surrounding tumor bed and the adjacent lymphatic tissues.

For many hundreds of years cautery and the use of escharotic materials were the main means of treatment of breast cancer. During the nineteenth century various modifications of simple mastectomy procedures were introduced. None of these measures was adequate to control breast cancer.

In 1894 Halsted[3] described an operation which was destined to become, after some modifications, widely accepted. Halsted did not at that time advocate removal of the pectoralis minor muscle. He did recommend removal of the supraclavicular lymph nodes on the same side as the breast lesion, but this was not routinely done. Meyer,[11] in 1894, presented an improved operation for radical mastectomy in which he advocated the routine removal of the pectoralis minor muscle as well as the pectoralis major muscle. These two great surgeons, independently concentrating on the problem of the surgical cure of breast cancer, were both arriving at essentially the same conclusions. Halsted also began to routinely remove the pectoralis minor muscle. He also described how some of his assistants removed the supraclavicular lymph nodes and explored the anterior mediastinum.

From 1920 to 1945 the most notable change in breast cancer therapy was the more widespread use of radium and x-ray therapy as primary treatment, as an adjunct to surgical operation and for palliation in inoperable cases. During the same period the use of estrogenic and androgenic hormones was introduced as an additional means of palliation.

The period from 1945 to the present has been one of confusing statistics, with many contradictory articles appearing in the literature, and no significant decrease in breast cancer mortality.

During this period, there have been extensive discussions of the question of simple mastectomy plus radiation therapy (McWhirter),[10] whether extended radical surgical procedures should be done, and the use of hypophysectomy and bilateral oophorectomy and adrenalectomy for palliative breast cancer. Also the importance of defining the various stages of the disease and of attempting to eliminate unnecessary operation in inoperable cases has been stressed.

It is surprising that, although much has been known for many years about the lymphatic drainage of the breast and in particular about the internal mammary lymphatics, not until recent years has a good deal of studious attention been given to this very important chain of lymph nodes. The supraclavicular lymph nodes have been ignored to a lesser degree. Most surgeons have considered involvement of the supraclavicular lymph nodes to indicate inoperability—probably rightly so, for the internal mammary lymph nodes are also usually involved.

It is quite apparent that without biopsy of the supraclavicular lymph nodes and the internal mammary lymph nodes, the clinical criteria of opera

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bility set forth by Steinthal and Portmann and as previously described by Haagensen, are entirely inadequate.

In a study of the regional breast lymphatic involvement Wyatt, Sugarbaker and Stanton[18] analyzed the results of extended radical operation in 60 cases of clinically operable breast cancer. They found that only the internal lymphatics were involved in seven cases and that both the axillary and internal mammary lymph nodes were involved in 12 additional cases. Routine radical mastectomy would have been ineffective in 19 of the 60 operated cases. They did not give data regarding the supraclavicular lymph nodes.

Urban[15] reported upon an analysis of 215 cases of radical mastectomy with en bloc resection of the internal mammary lymph node chain in continuity. There was one postoperative death. In 35 per cent of the cases the internal mammary lymph nodes were involved and in 50 per cent there was involvement of the axillary lymph nodes. In 7 per cent of the cases there was no extension beyond internal mammary lymph nodes. In 60 per cent of cases in which there was involvement of the axillary lymph nodes and the primary lesion was in the medial half of the breast, the internal mammary lymph nodes were involved; and there was internal mammary lymph node involvement in 40 per cent of cases in which the primary lesion was in the outer quadrant of the breast. In 42 per cent of Urban's cases, routine radical mastectomy would have been ineffective. Why biopsy of supraclavicular lymph nodes was not done was not stated, and it is possible that there may have been involvement of these nodes also in some cases. The incidence of supraclavicular lymph node involvement has been reported as high as 23 per cent.

MacGuffie[9] reported that, at Delafield Hospital, in 37.3 per cent of 371 cases of clinically operable breast cancer in which biopsy of internal mammary lymph nodes was done, involvement of the nodes was noted. At Presbyterian Hospital the proportion was 25.8 per cent of 450 such cases. In 110 cases biopsy of supraclavicular as well as internal mammary lymph nodes was carried out. In only two cases were the supraclavicular nodes involved without involvement of the internal mammary nodes. In 15 cases there was involvement of the internal mammary nodes but not the supraclavicular nodes.

Urban expressed belief that most of the lymphatic spread of breast cancer occurs by embolism rather than by permeation of the lymphatic vessels. He was also of the opinion that between 10 and 15 per cent of all primary breast cancers spread via the hematogenous route. Handley,[5] in 1922, believed that breast carcinoma spreads centrifugally in all directions from the point of origin by permeation of the lymphatic plexuses.

Any attempt to define the stages of breast cancer must depend upon pathological study. In the past, reports of methods of staging have made little mention of biopsy studies of the internal mammary lymph nodes. Realistic staging of operable breast cancer must be on a clinical, surgical and pathological basis. One must know the status of the lymph nodes in the supraclavicular, axillary and parasternal regions. There is increasing evidence that widespread metastasis may take place early in the course of the disease. Batson[1] described a system of vertebral veins which extend from the skull to the coccyx and it is possible that cancer cells may become widespread by passing through these veins without going through the lungs. Perhaps if bone marrow studies were done routinely on patients with mammary cancer the incidence of wide dissemination of metastatic cells would be found to be much higher than it is now thought to be.

Even if large firm nodes are palpable in the axilla, one must wait histological study before making a diagnosis. Haagensen and Stout[2] observed that in only 236 of 278 cases in which the axillary lymph nodes were thought to be involved, on the basis of clinical examination, was there microscopic evidence of metastasis. Hooper and McGraw[6] found microscopically demonstrable metastasis in only 111 of 145 cases in which there were palpable axillary lymph nodes. Conversely, in some 50 per cent of cases in which axillary nodes are not palpable before operation, metastatic cells are found upon examination of the excised nodes. It can be concluded that unless patients with breast cancer are operated upon and histological studies of the lymph nodes are carried out, no one can state with certainty whether or not the axillary lymph nodes are involved.

In a previous study, the author and co-workers,[13] utilized one of the accepted methods of defining the stages of breast cancer.* It was observed that approximately 50 per cent of the patients had inoperable cancer when first seen and in only about 20 per cent of cases was the lesion in Stage I. Eleven patients who had supraclavicular metastasis had radical mastectomy with dissection of the involved neck nodes, and none of them survived five years. It was thought to be a reasonable assumption that patients with supraclavicular metastasis probably have metastatic lesions elsewhere as well and are not suitable candidates for operation.

*Stage I, cancer confined to the breast; Stage II, cancer in the breast with metastasis to the axillary lymph nodes which are movable and with or without limited skin involvement of the breast; Stage III, fixation of the breast to the chest wall, metastasis to the supraclavicular lymph nodes, or distant metastasis.

Wangensteen and co-workers[16] reported the results of super-radical mastectomy done on 64 patients. The operation included excision of the supraclavicular, parasternal and mediastinal regional lymphatics. The operative mortality was 12.5 per cent. Thirty-seven or 57.8 per cent of the patients had metastatic cancer in the supraclavicular or mediastinal lymph nodes. Of 29 patients who were continuously observed, 17 were dead at the end of five years and only three of the remaining 12 were well.

Macdonald[8] expressed the belief that 55 per cent of patients with breast cancer have remote metastasis by the time the mammary lesions are detectable clinically, that in 20 per cent of cases the rate of growth is slow and the patients would live five years without treatment and that in the remaining 25 per cent of cases cure could be achieved by proper therapy, making a total of 45 per cent in which, theoretically, five-year survival would occur or could be brought about.

Urban[15] stated that the five-year salvage rate of patients with primary operable breast cancer treated by radical mastectomy is approximately 55 per cent in most of the large medical centers in this country. The five-year survival rate for 3,494 patients treated by radical mastectomy at the Memorial Hospital was 77.5 per cent in cases in which there was no axillary involvement and 39.4 per cent in cases in which axillary metastasis had occurred.

Handley and Thackray,[4] noting that "for the past 150 years isolated observers have been calling attention to the internal mammary lymph chain and its importance in the spread of carcinoma of the breast," but without offering convincing proof, began a study entailing biopsy of the internal mammary lymph node chain in association with routine radical mastectomy. Involvement of the internal mammary lymph nodes was noted in 41 of 139 patients (29 per cent) with "operable" carcinoma of the breast. In eight cases the internal mammary lymph nodes were involved without axillary invasion.

Whereas surgical treatment of breast cancer has been almost universally accepted, such has not been the case with radiation therapy.

During the past 20 years many improvements have been made in the techniques of therapy and particularly in the skill of the therapists. The work of McWhirter is an outstanding example of what can be done. Realizing that about 35 per cent of so-called "operable" breast cancers cannot be cured by the usual radical mastectomy because of internal mammary and supraclavicular lymph node involvement and that dissection of the axillary contents may actually spread the disease in some cases, McWhirter advocated simple mastectomy plus postoperative irradiation. He expressed belief that the metastatic lesions in the lymph nodes can be more readily destroyed by irradiation if the primary tumor is removed.

DISCUSSION

The extended or super-radical mastectomies will probably add little to the cure rate of breast cancer and there will be less need for them if radiation therapists and surgeons will work together to develop an effective regimen of therapy.

In the past it has not been uncommon for some surgeons to do inadequate operation and then refer the patient for radiation in the hope that any remaining cancer cells would be destroyed. While radiation therapy may in some cases and to some degree compensate for inadequate excision, it ought not be relied upon for this purpose.

The radiation therapist must be competent and willing to assume the responsibility for carrying out thorough adequate radiation therapy. It is difficult to sterilize breast cancer by radiation therapy, but it can be done. It may not always be necessary to sterilize all the cancer cells, for the effect of the radiation is not only directly upon the cancer cell but on the tumor bed also. The inherent resistance or immunity of the host against the cancer may be increased. Cases in point are two in which there was recurrence, in the surgical scar, long after radical mastectomy—21 years in one case, 32 in the other. It must be assumed that the cancer cells were lying dormant all those years until something happened to the host's natural resistance and the cancer cells began to grow again.

If radiation therapy is to be given probably the most controversial question is whether it is to be used preoperatively or postoperatively. I do not believe that sufficient evidence is available to justify the assumption that preoperative is superior to postoperative radiation therapy. Personal experiences with preoperative radiation have not justified its continued use. Giving radiation therapy before operation delays the removal of the primary lesions and on the other hand operation may be carried out too soon afterward to permit the maximum benefit from radiation.

Stein and co-workers[13] presented data to the effect that radical mastectomy and postoperative radiation materially increased the five-year survival rate. There are many reports in the literature by other investigators who have reached similar conclusions.

Surgical treatment is superior to irradiation for "operable" breast cancer when it is the only method of therapy to be used. Although the majority of surgeons in this country today may advocate radical mastectomy as the only method by which breast cancer can be successfully treated, newer concepts

in breast cancer therapy may change this attitude, particularly in light of the previously mentioned facts that the breast cancer mortality has not declined, that the internal mammary lymph nodes and the supraclavicular lymph nodes may also be involved in a large proportion of cases, that it is impossible to determine operability without biopsy of these nodes, and that the extended radical mastectomy operation also leaves much to be desired.

Surely, then, the radiation therapist has much to offer in dealing with patients who have mammary cancer if a planned program is worked out in cooperation with surgeons and pathologists. At St. Bartholomew's Hospital approximately one-half of the patients admitted with breast cancer are treated by radical mastectomy and about one-half by conservative operation and radiotherapy. The results of study of these cases will be reported after a sufficient number have been treated and observed long enough.[17]

Operations, such as hypophysectomy, bilateral oophorectomy and adrenalectomy, and the use of estrogenic and androgenic hormones are of considerable importance for palliation in far advanced breast cancer. However, criteria for determining the selection of patient and the optimum time for operations of the kind mentioned are not yet definitely established.

Castration, either by operation or by radiation, offers additional months of palliation to a relatively high proportion of patients with far advanced breast cancer.

Hormones now have been used long enough in the treatment of advanced cancer of the breast to permit conclusion that they are of considerable value. The estrogens are usually prescribed for postmenopausal and the androgens for pre-menopausal women. It is probably preferable to use each palliative measure to its fullest extent rather than combine two or more at one time. For example, castration may be beneficial for four to nine months, and then later hormonal therapy could be used.

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Social Security Footnotes

THE LATE Robert A. Taft classified the Social Security Act as our greatest single step toward socialism.

—From the Department of Public Relations, American Medical Association

Triiodothyronine

Clinical Effects in Patients with Suboptimal Response to Other Thyroid Preparations

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• Thirty patients with evidence of hypometabolism or a clinically related condition were given triiodothyronine after suboptimal response to thyroxin or desiccated thyroid. DL- and L-isomers of triiodothyronine were used and compared. Thirteen patients (43.3 per cent) were improved and 17 (56.6 per cent) were unimproved or became worse. Side effects occurred in 9 of 34 trials (26 per cent), and could not always be eliminated by decreasing the dosage. The highest percentage of good response occurred in a small group (four of five) who received a combination of desiccated thyroid or thyroxin with supplemental triiodothyronine. Despite careful analysis of the data, no basis was found on which to predict which patients would receive benefit from the triiodothyronine. However, the occasional improvement, sometimes dramatic, suggested that a therapeutic trial with triiodothyronine in difficult or unresponsive cases of hypometabolism or hypothyroidism is justified.

IT IS WELL KNOWN that the usual patient with hypothyroidism is improved dramatically by replacement therapy with desiccated thyroid or thyroxin. However, occasional patients do not respond completely, and some with lowered metabolic rates have little improvement or significant side effects from usually adequate doses. In such persons the most common complaints are fatigue, lethargy, tendency to gain weight easily, nervousness, irritability, skeletal pains, emotional instability and sensitivity to cold.[3,6] The basal metabolic rate may be low, but results of other tests of thyroid function are usually within normal ranges. Large doses of desiccated thyroid may be necessary to raise the basal metabolic rate, but clinical benefit is not adequate or permanent, and side effects may prevent increasing the dose to what may seem to be a desirable level.

With the synthesis in 1952 of 3:5:3′-L-triiodothyronine,[2] a new therapeutic tool seemed available for trial in cases of this type. This new substance was found to be three to five times as potent as L-thyroxin,[1,6] with the levo form being 15 times as potent as the dextro isomer.[1,6] Therefore, 50 mcg. tablets of DL-triiodothyronine (Trionine®) as used in this study, containing both isomers, have the apparent clinical effect of 25 mcg. tablets of L-triiodothyronine (Cytomel®). In order to avoid confusion, the former (Trionine) is now labeled 25 mcg. according to its content of the L-form. In trial, 50 to 60 mcg. of DL-triiodothyronine, or 25 to 30 mcg. of L-triiodothyronine had a clinical and calorigenic effect approximately equal to 65 mg. of desiccated thyroid or 0.1 mg. of L-thyroxin.[1,4,6] Triiodothyronine acts more quickly and the effects are of shorter duration (24 to 48 hours) than those of thyroxin (two to three weeks) or of desiccated thyroid, which apparently contains both elements.

Recent reports have indicated that the rapidly acting triiodothyronine is occasionally more effective than desiccated thyroid,[1,3] especially when results with the latter were not satisfactory. However, some caution is indicated because of the rapid onset of side effects, including those on the cardio-vascular system (palpitation, angina) as well as headaches and nervousness. However, following withdrawal of triiodothyronine, there is earlier loss of undesirable effects or quicker relapse into an hypothyroid state than with thyroxin or thyroid. Clinical improvement in cases of myxedema has been associated with an increase in the basal metabolic rate and a lowering of the blood cholesterol, although the protein-bound iodine remains at hypothyroid levels.[5]

MATERIALS AND METHODS

Over a period of two years, Trionine (DL-triiodothyronine) and Cytomel (L-triiodothyronine) were administered to 30 patients observed in the Endocrine and Isotope Clinics of the Letterman Army Hospital and in private practice. Twenty-six of the patients were females and four were males. The age range was from 14 to 64 years. All but three had taken thyroid preparations for over one year in daily doses ranging from 0.12 to 0.55 grams (2 to 8 grains) of desiccated thyroid or equivalent.

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Twenty-four had taken more than 0.2 gm. (3 grains) a day for more than a year, and those taking less were unable to tolerate an increase in dosage. However, all continued to have symptoms, physical findings or laboratory results suggesting persistent hypometabolism, or significant side effects that prevented further increase in dosage of thyroid preparations. Whenever possible, a dose of triiodothyronine at least equivalent to the previously administered dose of thyroid was given, so that the effects could be compared.

For this study, Trionine (DL-triiodothyronine) was supplied in tablets of 50 mcg. (later labeled 25 mcg. according to content of L-triiodothyronine), and Cytomel in tablets of 5 mcg. and 25 mcg.* Some of the patients received Trionine and Cytomel at different times, and others were given a combination of one of the triiodothyronine preparations along with thyroxin or desiccated thyroid. One patient discontinued triiodothyronine after a few days because of side effects, three were treated for one month, and the remainder for two months or more before the therapeutic effect was evaluated. Eight patients were treated with triiodothyronine for at least six months and two for over one year.

Table 1 gives the details regarding the individual patients—the significant symptoms, physical findings, laboratory tests, medications and results. Also an attempt is made to compare the benefits from the various plans of therapy.

RESULTS

For the 30 patients treated, the results were as follows:

Unimproved—17 patients (56.6 per cent) were no better or they became worse while receiving triiodothyronine than they were previously while receiving desiccated thyroid or thyroxin.

Improved—13 patients (43.3 per cent) were better in varying degrees than they had been while receiving previous therapy.

Trionine (DL-triiodothyronine) was administered to 23 patients, 18 of whom were not improved, two somewhat improved and three much improved.

Cytomel (L-triiodothyronine) was administered to 11 patients, four of whom showed no improvement, six definite improvement and one only temporary improvement.

Trionine and Cytomel. Effects were compared in the same patient in six instances. Three felt that Cytomel was more effective, one that Trionine was superior, and two that they were not improved by either.

Combination therapy. Three patients received Trionine in combination with thyroxin or desiccated thyroid. Two received Cytomel plus thyroid. Four of the five patients receiving combined therapy derived significant benefit.

Side effects. Side effects occurred in nine of 34 trials (26 per cent); eight in the 23 patients receiving Trionine (35 per cent), and one in the 11 patients given Cytomel (9 per cent). Nervousness, palpitation and headache were the principal complaints. These effects could sometimes, but not always, be ameliorated by adjustment of dosage. One patient reported that increased nervousness occurred within two hours after the medication (Trionine) was taken and was followed by a "let-down" after four hours.

Comparison with previous therapy. As was previously noted, improvement occurred in 13 patients, ten noted no difference (seven taking Trionine and three Cytomel), and seven (six on Trionine, one on Cytomel) had results less satisfactory than that obtained formerly with desiccated thyroid or Proloid.

DISCUSSION

Patients of the kind dealt with in this study are often the subject of clinical speculation. Opinions vary as to whether the cause of the difficulty in individual cases may be physiological hypometabolism, end-organ insensitivity, rapid inactivation or diminished absorption of the thyroid hormone,[3] a mild or bizarre form of hypothyroidism not measurable by available tests of thyroid function. Another possibility is that the symptoms are independent of the apparent hypometabolism and result from an entirely different process. In an attempt to alleviate persistent symptoms, a physician may prescribe increasing doses of desiccated thyroid over a period of years without full relief, and frequently to the point of undesirable side effects. This study suggests that triiodothyronine may offer some hope of further improvement in slightly less than half of these cases.

Improvement was based on a comparison with the patient's previous response to thyroid medication, which was considered as a control period. Since desiccated thyroid is inexpensive and easy to administer, the newer triiodothyronine preparations would be preferable only if they resulted in greater benefit to the patients. A satisfactory response (+) was recorded when complete or definite improvement occurred on change to the new medication without annoying side effects. Slight benefit (±) indicated a diminution but persistence of symptoms. No benefit (0) indicated either no effect or that the patient became worse after the change of medication.

*Trionine was supplied by Dr. R. J. Floody of Hoffmann-LaRoche, Inc., and Cytomel by Dr. H. A. Klusek of the Smith Kline and French Laboratories.

TABLE 1.—*Clinical and Laboratory Data on 30 Patients with Evidence of Hypothyroidism Who Were Treated with Triiodothyronine After Suboptimal Response to Thyroxin or Desiccated Thyroid.*

Case	Age and Sex	Significant Findings	Treatment	Maximum Dose	Duration	Studies: BMR Per Cent	Studies: Cholesterol mg. per 100 cc.	Studies: PBI mcg. per 100 cc.	Studies: I^{131} Uptake Per Cent	Benefit: *Tx.	Benefit: TriTh.	Side Effects: Tx.	Side Effects: TriTh.	Remarks and Conclusions
1.	47 F 1953	Fatigue, mental sluggishness, and obesity while on thyroid.	Thyroid Cytomel Trionine	260 mg. (4 gr.) 100 mcg. 200 mcg.	5 Yr. 3 Mo. 1 Mo.	— 5	165			0	+ 0	0	± +	Cytomel better than Trionine or thyroid.
2.	42 F 1937	Fatigue, obesity, sensitivity to cold, dry skin, hair loss while on thyroid.	Thyroid Trionine	423 mg. (6.5 gr.) 350 mcg.	19 Yr. 8 Mo.	— 1	222 to 350 306	4.4-5.8 0.8	21 (after TSH)	±	0	±	+	ECG normal. ECG low voltage; nervous 2 hr. after dose, "letdown" 4 hr. after. Thyroid better than Trionine.
3.	31 M 1937	Fatigue, constipation, drowsiness, impaired memory while on thyroid.	None Thyroid Trionine	260 mg. (4 gr.) 200 mcg.	18 Yr. 10 Mo.	—24 — 8 to —22	215 to 330			±	± ±	±	±	Trionine no better than thyroid.
4.	21 F 1954	Fatigue, metrorrhagia while on thyroid.	Thyroid Trionine	260 mg. (4 gr.) 150 mcg.	6 Yr. 9 Mo.	—18 + 2	191 135			±	0	0	0	Trionine not as good as thyroid.
5.	16 M 1956	Fatigue, poor grades in school, sensitivity to cold, weight gain while on thyroid.	None Thyroid or Proloid Trionine	325 mg. (5 gr.) 200 mcg.	4 Yr. 9 Mo.	—20, —27 — 7	183 to 200 175	2.0, 2.5		0	+ 0	0	± ±	Trionine dramatically better than thyroid or Proloid.
6.	45 F 1953	Postoperative hypothyroid, fatigue, headaches, dry skin while on thyroid.	Thyroid Trionine Cytomel	260 mg. (4 gr.) 200 mcg. 150 mcg.	4 Yr. 4 Mo. 4 Mo.	—16 —13	220 161			±	0 +	0	0 0	Cytomel better than Trionine or thyroid, but comparable doses were not used.
7.	53 F 1953	Postoperative hypothyroid, side effects from thyroid, fatigue, pulse 60, puffy lids while on small doses of thyroid.	None Proloid Trionine Trionine & Thyroxin	130 mg. (2 gr.) 75 mcg. 50 mcg. + 0.5 mg.	1 Yr. 2 Mo. 2 Mo.	—12 —19 + 4	225 191 170			0	0 +	+	+ 0	Trionine plus thyroxin better than either Trionine, Proloid or desiccated thyroid alone.
8.	45 F 1949	Menorrhagia, fatigue, dry skin, pallor.	None Thyroid Trionine	260 mg. (4 gr.) 200 mcg.	6 Yr. 3 Mo.	—22 — 7 to —18	233 205 to 295			±	0	0	0	Trionine not as effective as thyroid.
9.	43 F 1949	Muscle cramps, irregular periods, tachycardia, dry skin.	None Thyroid Trionine	325 mg. (5 gr.) 250 mcg.	7 Yr. 5 Mo.	—14				±	0	0	0	Trionine not as effective as thyroid.
10.	34 F 1955	Fatigue, sensitivity to cold, puffy lids. Hashimoto's Struma with postoperative hypothyroid while on thyroid.	None Proloid Cytomel	130 mg. (2 gr.) 25 mcg.	2 Yr. 4 Mo.	—27 — 2 to —18	170	3.1		±	0	0	+	Cytomel not as effective as Proloid.
11.	18 F 1956	Fatigue, constipation, irregular periods while on thyroid.	None Thyroid Cytomel Trionine	325 mg. (5 gr.) 25 mcg. 250 mcg.	7 Yr. 3 Mo. 2 Mo.	—45 —16	153			0	0 0	0	0 0	Neither Cytomel nor Trionine more effective than thyroid. Cytomel dose small.
12.	45 M 1956	Fatigue, dry skin, constipation while on thyroid.	None Thyroid Trionine Trionine & Synthroid Cytomel & Synthroid	325 mg. (5 gr.) 200 mcg. 200 mcg. + 0.1 mg. 100 mcg. + 0.1 mg.	7 Yr. 6 Mo. 4 Mo. 2 Mo.	—21 to —17	220	2.5		0	0 + 0	0	0 0 0	Trionine plus Synthroid better than Trionine or thyroid alone or Cytomel plus Synthroid.
13.	46 F 1955	Postoperative hypothyroid, dry skin, dyspnea while on thyroid.	None Thyroid Cytomel	260 mg. (4 gr.) 100 mcg.	3 Yr. 2 Mo.	—25 —10 to —27	170			±	0	0	0	Cytomel no better than thyroid.
14.	18 F 1947	Obesity, fatigue, slow pulse, dry skin, mentally sluggish.	None Thyroid Trionine	260 mg. (4 gr.) 150 mcg.	4 Yr. 4 Mo.	— 9 to —18 —11, +6	220, 233 233			0	+ +	0	0 0	Trionine better than thyroid.

	1947		skin, mentally sluggish.	Thyroid Trionine	260 mg. (4 gr.) 150 mcg.	4 Yr. 4 Mo.	—11, +6	233				0	+ 0	0	0		

15.	45 1955	F	Fatigue, obesity, edema, dry skin while on thyroid.	Thyroid Trionine Trionine & Thyroid	390 mg. (6 gr.) 300 mcg. 300 mcg. 120 mg. (2 gr.)	25 Yr. 1 Yr. 3 Mo.	+18 + 7	149 149				0	0 +	0	0		Only temporary benefit from Trionine. Trionine plus thyroid most effective.
16.	64 1955	F	Obesity, dry skin, puffy lids while on thyroid.	None Thyroid Cytomel Trionine	 162 mg. (2.5 gr.) 75 mcg. 150 mcg.	 1½ Yr. 3 Mo. 3 Mo.	—16	185				0	+ 0	+	0 0		Cytomel better than thyroid or Trionine.
17.	14 1954	F	Obesity, fatigue, irregular periods, rough skin.	None Thyroid Cytomel	 260 mg. (4 gr.) 75 mcg.	 1 1/3 Yr. 10 Mo.	—19 —11	165 153				0	0	0	0		Cytomel originally beneficial but later had no effect.
18.	16 1953	F	Obesity, nervousness, irregular periods, slow pulse.	None Thyroid Trionine	 260 mg. (4 gr.) 150 mcg.	 2½ Yr. 5 Mo.	—28 — 8 to —30	207 230				0	0	0	0		Trionine no better than thyroid.
19.	51 1954	M	Fatigue.	None Thyroid Trionine	 260 mg. (4 gr.) 150 mcg.	 2 Yr. 4 Mo.	—30 —29	191 215				0	0	0	+ +		Trionine no better than thyroid. Trionine caused marked headaches and nervousness.
20.	32 1955	F	Fatigue, obesity, constipation, vertigo.	Thyroid Cytomel Trionine Cytomel & Thyroid	260 mg. (4 gr.) 75 mcg. 150 mcg. 50 mcg. 260 mg. (4 gr.)	1 Yr. 3 Mo. 1 Mo. 11 Mo.	—26 —34 — 3	181 217 205				0	0 0 ±	0	0 0 0		Cytomel or Trionine no better than thyroid. Cytomel plus thyroid slightly better than either alone.
21.	19 1954	F	Obesity, had taken thyroid for ten years.	Thyroid Trionine	195 mg. (3 gr.) 150 mcg.	11 Yr. 6 Mo.	+ 2 to —16 —13	120				0	+ +	0	0		Trionine better than thyroid.
22.	49 1955	F	Fatigue, dry skin.	None Thyroid Trionine	 65 mg. (1 gr.) 50 mcg.	 7 Mo. 1 Mo.	—13 + 9	220	5			0	0	+	+ +		Both Trionine and thyroid produced side effects without apparent benefit.
23.	42 1952	F	Fatigue, numbness, sensitivity to cold, slow reflexes, thin brows.	None Thyroid Trionine	 32 mg. (0.5 gr.) 25 mcg.	 2 Mo. 3 Days	—17, —24	219, 263	3.2	39		0	0	+	+ +		Both Trionine and thyroid caused side effects without apparent benefit.
24.	47 1955	F	Fatigue, weakness, sensitivity to cold, slow pulse, puffy lids, slow reflexes, low voltage of ECG while on thyroid.	None Thyroid Trionine	 260 mg. (4 gr.) 200 mcg.	 7 Yr. 5 Mo.		 135 241	 3.3	3.1 & 1.1 (after TSH)	±		± ±	0	0		Slight response to Trionine or thyroid.
25.	54 1954	F	Postoperative hypothyroid, fatigue, nervousness, weight gain while on thyroid.	Thyroid Trionine	260 mg. (4 gr.) 200 mcg.	12 Yr. 5 Mo.	+ 5 +38	226 295	5.9	18 (after TSH)	±		± 0	±	+ +		Trionine caused more side effects and not as beneficial as thyroid.
26.	38 1951	F	Obesity, rough skin, fatigue while on thyroid.	None Thyroid Cytomel	 520 mg. (8 gr.) 75 mcg.	 20 Yr. 2 Mo.	—35 —17 to +50	153				0	+ +	+	0 0		Cytomel much better than thyroid.
27.	39 1937	F	Obesity, fatigue, headaches, rough skin, coarse hair while on thyroid.	None Thyroid Cytomel	 65 mg. (1 gr.) 50 mcg.	 35 Yr. 4 Mo.	—18 to —32 — 5 to —16	215				0	+ +	+	0 0		Side effects from small doses of thyroid. Cytomel better than thyroid.
28.	37 1956	F	Fatigue, dry skin while on thyroid.	None Thyroid Thyroid & Cytomel	 520 mg. (8 gr.) 180 mg. (3 gr.) 25 mcg.	 8 Yr. 3 Mo.	—10 to —21 +15	260	3.3		±		+ +	+	0 0		Cytomel and thyroid better than thyroid alone.
29.	48 1955	F	Fatigue.	None Thyroid Cytomel	 195 mg. (3 gr.) 75 mcg.	 14 Mo. 2 Mo.	—17 to —30 —19 — 8	205 165			±		0 +	+	± ±		Cytomel better than thyroid.
30.	24	F	Fatigue, listlessness, obese, dry skin while on thyroid.	None Thyroid Trionine	 422 mg. (6.5 gr.) 200 mcg.	 16 Yr. 4 Mo.	—30 +10, +38	 190	 2.1	0 & 1 (after TSH)	±		± 0	±	+ +		Thyroid better than Trionine and fewer side effects.

*Tx. represents dessicated thyroid, thyroxin or similar preparations.
TriTh. represents triiodothyronine.

+ = Satisfactory response. ± = Slight benefit. O = No effect or patient became worse.
(When symbol is midway between columns, it applies to a combination of both drugs.)

PBI = Protein-bound iodine.
BMR = Basal metabolic rate.

TSH = Thyroid stimulating hormone.

Laboratory studies were not helpful in predicting or judging response to therapy. Five patients with satisfactory response all had normal basal metabolic rates and four had serum cholesterol content within normal limits. Serum cholesterol was determined in four of five others who did not respond; three of them had normal levels, and the basal metabolic rate was normal in one of the three patients tested. The protein-bound iodine and radioiodine uptake are not reliable tests during triiodothyronine therapy.

In general, a beneficial result was associated with an improvement in the basal metabolic rate and cholesterol content if these were initially abnormal or borderline. If the tests were initially normal, improvement occasionally occurred without a change in the measurable thyroid function. The criteria for improvement were based mainly on the effect on symptoms and physical findings. This clinical improvement seemed definite and at times dramatic in previously unresponsive and difficult patients. The possibility that improvement was due to suggestion was considered but seemed unlikely because most of the patients had been observed for long periods while taking thyroid medication of other types and had not had significant improvement.

In this series, results were somewhat better with the levo isomer, but the number of patients is too small to permit drawing definite conclusions in this regard.

Four of the five patients who received combination therapy showed definite improvement. It seems possible that the slower and smoother action of desiccated thyroid or thyroxin was improved by the added rapid stimulatory effect of triiodothyronine.

We recognize that this group of patients probably represents a mixture of several conditions, including hypothyroidism, hypometabolism without myxedema, and functional complaints not related to hypometabolism. Since fewer than half showed improvement over the effects of previous therapy, a careful analysis of the symptoms, physical findings and laboratory results was made. However, no common factor was found which would be helpful in predicting which patients would be improved by a change to or addition of triiodothyronine (which costs more). Improvement did occur often enough to suggest that a therapeutic trial with triiodothyronine is worthwhile in patients who apparently need desiccated thyroid but do not have satisfactory response to it.

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No. 1 Killer

The National Safety Council has put one automobile man among its 33 trustees and one among its 44 directors. Yet motor vehicles account for 42 per cent of all fatal accidents.

Cigarette Smoke

Its Effect on Pulmonary Function Measurements

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• **Inhaling cigarette smoke with each breath, with the subject at rest, by use of a smoking device that brought more smoke into the lungs than would be the case in ordinary smoking, produced consistent significant decreases in arterial blood oxygen saturation and in arterial pO_2 in most subjects who had severe or very severe pulmonary emphysema. In normal subjects and in those with a moderate degree of emphysema no significant changes in blood gas exchange resulted.**

No consistent significant changes in blood gas exchange were noted after the smoking of two cigarettes, either with the subject at rest or after a one-minute step-up exercise.

A decrease in oxygen uptake occurred when treadmill exercise was done after smoking two cigarettes, and the ventilation volume was also decreased, probably accounting for part of the oxygen decrease.

Pulmonary compliance measurements after smoking one cigarette were consistently and significantly decreased in most subjects—normal as well as those with pulmonary emphysema. The elastic work of breathing was increased in the majority of cases.

In two cases in which studies were done after the subjects stopped smoking, one for three months and one for two years, significant reductions in residual air were noted.

The results indicated that persons with severe or very severe emphysema would be better off to stop smoking.

THE RELATIONSHIP of chronic pulmonary disease, such as emphysema, and smoking is of particular interest in the Cardio-Respiratory Laboratory of the University of Southern California School of Medicine. A very high incidence of cigarette smoking has been noted commonly in the history of patients with severe emphysema when there was no apparent cause for the emphysema, such as a history of exposure to silica, asbestos, diatomaceous earth or other known irritating dusts, or a history of having had tuberculosis, asthma or some other chronic pulmonary disease.

Some physicians have arbitrarily ordered patients to stop smoking as part of the management of pulmonary emphysema. On the other hand, other physicians do not even advise patients with emphysema to stop smoking.

The Cardio-Respiratory Laboratory is frequently asked for an opinion as to whether or not a patient should stop smoking, and if so, what is the objective evidence. If pulmonary function measurements were to show definite and significant changes impairing lung function as the result of smoking, then it would be much easier to convince patients with emphysema that they should give up smoking.

Pulmonary emphysema may be the result of several factors and the evaluation of the importance of each one may be quite difficult. The present study was set up to explore the practical tests of pulmonary function which might be used to assess acute changes which could be induced by smoking one or two cigarettes, and thus permitting each subject to serve as his own control. The subjects studied were all smokers and the group included persons without disease and patients with chronic pulmonary disease of varying degrees of severity, especially pulmonary emphysema and pulmonary fibrosis. The subjects were advised to abstain from smoking from four to six hours before the tests of function were to be done, and in a few cases for as long as twenty-four hours. A longer time interval without smoking would be desirable; and it would also be helpful to obtain studies before and during the period of abstinence, and after resuming smoking. However, obtaining volunteers for such restrictions would be difficult. In two cases, follow-up studies were obtained after longer time intervals, as the patients decided to stop smoking; and as far as could be determined, no medication had been taken during this time which might be a factor in altering the pulmonary function measurements.

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Supported by a research grant from Tobacco Industry Research Committee, 150 East Forty-Second Street, New York 17, N. Y.

Presented before the Section on Allergy at the 86th Annual Session of the California Medical Association, Los Angeles, April 28 to May 1, 1957.

METHODS

All the subjects—125 men and 16 women—were fasting and in an essentially basal state at the time of the studies. The ages ranged from 24 to 70 years. Each of the subjects had a complete pulmonary function evaluation including lung volume de-

terminations and blood gas exchange measurements while at rest and after exercise (except for three subjects who had heart disease and one normal subject).

Spirogram recordings on the 13.5 liter respirometer were made to determine the total vital capacity, the timed vital capacity for three seconds and the maximal breathing capacity, before and after administration of a bronchodilator drug.[12] Residual air was measured by the oxygen open circuit method and the helium closed circuit method.[13] The residual measurements were made with the subject supine in a fasting and resting state. The alveolar nitrogen sample was taken just above the mouthpiece after seven minutes of oxygen breathing. In a few cases, the nitrogen curve was obtained after a single deep breath of oxygen, using the nitrogen meter. The nitrogen wash-out was also obtained in a few of these subjects with the nitrogen meter with continuous recordings. All lung volume measurements were expressed at body temperature, pressure saturated (BTPS).

Arterial blood samples were obtained through an indwelling needle from the brachial artery, at rest and immediately after exercise. Oxygen content and capacity and carbon dioxide content determinations were made in duplicate by two trained technicians using different manometric Van Slyke analyzers and were repeated unless the results were close together. The arterial blood oxygen saturation (as per cent) was also determined on the Water's oximeter, double scale cuvette with the use of whole blood. The cuvette was calibrated daily against the Van Slyke analyzers, and in this laboratory it has been found very satisfactory, the results consistently staying within one per cent of the Van Slyke measurements when properly calibrated. The pH was measured on a Cambridge glass electrode. The arterial partial pressure oxygen (pO_2) and partial pressure carbon dioxide (pCO_2) were determined by the direct bubble tension method described by Riley.[15]

Oxygen uptake and carbon dioxide output were calculated from the percentage of oxygen and carbon dioxide in the expired air, as determined in a Scholander gas analyzer. The step-up exercise consisted of stepping up and down on a stool, 20 cm. high, 30 times in one minute; and the treadmill exercise was walking, level, at a rate of two miles per hour. The minute ventilation volume was measured during the basal rest period and during the one minute of step-up exercise, or during the sampling period on the treadmill after five minutes or more of walking. The minute ventilation and the oxygen uptake were expressed at standard temperature and pressure as liters per minute, or milliliters per minute per square meter of body surface area (ml./min./M^2, BSA). The alveolar pO_2 was calculated from the values obtained for arterial pO_2, the arterial pCO_2 and the respiratory quotient. The effective tidal air was calculated from the expired pCO_2 and the arterial pCO_2 using the average tidal volume. Hemoglobin was determined both by the oxygen capacity method and by converting all the hemoglobin to cyanmethemoglobin[8] and measuring light absorption at 540 mu. on the Beckman DU spectrophotometer.

Measurements of pulmonary compliance were determined by the continuous cycling method with modifications.[9] The recording device consisted of a 6-liter Benedict-Roth metabolism apparatus equipped with a helipot for volume changes. A blower was provided in the circuit to circulate the air, and all valves were removed to reduce breathing resistance. Oxygen was added to the system and the CO_2 was absorbed. Volume and pressure changes were recorded on a DuMont cathode ray oscilloscope through a compliance control apparatus employing a capacity transducer in a radio frequency circuit. The loop was interrupted by means of a blanking generator which allowed time measurements of 5, 10, 15 and 20 cycles per second intervals. In addition, the points at which there was no flow were determined by a flow-sensitive zero pressure device which produced blips on the oscilloscope at the end of expiration and inspiration. A balloon as described by Crane[7] was used to measure the intraesophageal pressure at its mid-position. The loop was then photographed with a polaroid Land camera. The patients were studied in the sitting position during spontaneous quiet breathing before and immediately after smoking one cigarette.

PROCEDURE AND SUBJECT MATERIAL

Studies were obtained on nine patients, all except two with severe pulmonary emphysema, in the supine position after smoking two cigarettes. The amount of smoke inhaled varied widely between different subjects during the smoking of two cigarettes; some inhaled deeply, others hardly at all.

It was felt that the acute effects of cigarette smoke on the lung could be intensified by the use of a smoking device so that with each breath some smoke would be inhaled in the lung with the respiratory gases. The subject was connected by a mouthpiece to a two-way directional valve which was connected on the intake side to a Douglas bag containing air on one side of a "Y" tube and on the other side containing a cigarette holder with a lighted cigarette. By the use of a three-way valve attached to the Douglas bag, the resistance could be varied so that a small amount of air with each breath was directed through the cigarette, with a resulting glow during

inspiration. The expired air was collected in a Tissot gasometer and the smoke was quite visible in the expired air from the subject.

In some subjects the inhaled smoke produced a sensation of burning, particularly on the posterior pharynx, and in a few it caused cough. Other subjects, most commonly heavy smokers with a history of smoking for many years, said that they were not aware that they were even getting smoke with the device. The use of the smoking device in the closed circuit insured that the smoke was distributed in the lung, so that the effect of smoke on the lung with respect to blood gas exchange could be studied. In all instances, the patients were allowed to smoke the cigarette of choice if they had their own. The rate of smoking was set so that usually it took about three to five minutes to completely smoke one cigarette, and in most instances at least 90 per cent of the cigarette was smoked. Fifty subjects were studied during the smoking of one cigarette, and these subjects were divided into three groups according to the severity of the pulmonary emphysema present. There were 23 cases in which the emphysema was insignificant, eight in which there was a moderate degree of emphysema and 19 in which it was severe or very severe (residual air greater than 45 per cent of total lung capacity).

Pulmonary compliance measurements were obtained on 41 subjects. In these subjects the residual per cent of total lung capacity had been determined (with the exception of three subjects who had cardiac disease and one who was normal). The vital capacity was determined in most of the subjects before and after smoking, utilizing the usual volume recording apparatus, but with the subjects in the sitting position. Compliance and the elastic work of breathing were the two specific measurements obtained at this study, and these data were correlated with the severity of the emphysema as measured by the residual per cent of total lung capacity, the ventilation factor, the resting arterial pO_2 and the vital capacity, before and after smoking.

A group of fifty subjects had blood gas exchange measurements made before and after smoking, using the one minute step-up exercise test. This group of fifty subjects was divided into three classes, depending on the severity of the emphysema. There were 19 with an insignificant degree of emphysema, 16 with a moderate degree of emphysema and 15 with a severe or very severe degree of pulmonary emphysema. The second exercise test was performed immediately after smoking two cigarettes and the measurements were compared to those of the first test. In 21 cases, treadmill exercise was used instead of step-up exercise, and the blood gas exchange measurements before and after smoking two cigarettes were compared.

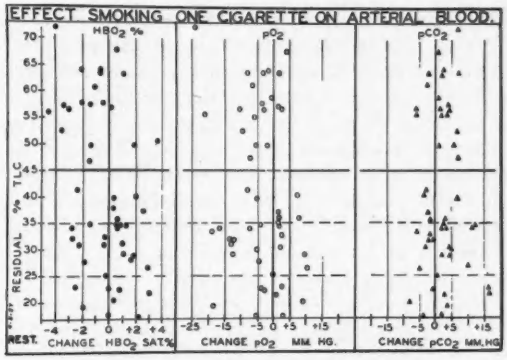

Chart 1.—Correlation of the residual per cent of total lung capacity with the change during the smoking of one cigarette with the smoking device, at rest, on: (1) Arterial blood oxygen saturation (HbO_2 saturation, per cent, (2) arterial pO_2, and (3) pCO_2 in mm. Hg., both by direct tension measurement. TLC (total lung capacity), HbO_2 per cent (arterial oxygen saturation, per cent), pO_2 (partial pressure oxygen), pCO_2 (partial pressure carbon dioxide). Measurements on 50 cases.

RESULTS

Blood gas studies in the supine position before and after smoking two cigarettes were obtained in nine subjects, seven of whom had severe emphysema. There was no significant average difference after smoking in the group, as shown by the arterial blood or the pulmonary ventilation measurements.* There was a slight increase in the pulse rate, but no significant change in the respiratory rate. In one subject at rest there was a significant decrease (—6.5 per cent) in the arterial blood oxygen saturation after smoking. This subject had a very severe degree of emphysema, and following the smoking the pulse rate, respiration rate and minute ventilation were significantly increased, but the arterial pO_2 was decreased from 73.5 to 56.1 mm. of mercury.

The smoking device with the closed circuit was next used in the supine position to insure that the smoke from the cigarette got into the lung. The data using the smoking device were compared in summary form by three groups based on the severity of the emphysema. There was no significant change in the arterial blood oxygen saturations before and after smoking either in the nonemphysema group or in the group with a moderate degree of emphysema. However, in the severe emphysema group there was an average decrease in the arterial blood oxygen saturation from 90.7 per cent at rest to 88.6 per cent after smoking. The changes in the arterial blood saturation before and after smoking have been plotted for each case on a basis of the severity of the

*More detailed data in tabular form will be published in the reprint of this paper.

emphysema as measured by the residual per cent of total lung capacity (Chart 1). It can be noted that none of the subjects with a residual per cent of total lung capacity below 45 per cent had significant change. In some the saturation was increased a little and in others it was decreased. However, in this group of 19 subjects with severe or very severe pulmonary emphysema there was definitely a decrease in the saturation after smoking, a decrease occurring in 14 and an increase in four, with no change in one. The standard deviation for the 19 subjects was ± 1.96 per cent with a standard error of 0.45 per cent. In a similar manner, the arterial pO_2, as determined by direct tension measurement, was correlated with the severity of the pulmonary emphysema (Chart 1), and a consistent decrease was present only in subjects with a residual ratio greater than 45 per cent of total lung capacity (decreased in all except four). The standard deviation of the arterial pO_2 was ± 7.6 mm. of mercury with a standard error of 1.7 mm. of mercury. When the arterial pCO_2 was correlated with the residual per cent of total lung capacity, it was noted that in the emphysema group in all except four cases there was an increase after smoking. The standard deviation of the arterial pCO_2 was ± 2.0 mm. of mercury with a standard error of 0.9 mm. There was no significant change in the arterial CO_2 content or pH after smoking with the smoking device. Also the alveolar-arterial pO_2 difference was not significantly changed after smoking. The mean alveolar pO_2 was calculated from the arterial pCO_2, the arterial pO_2 and the respiratory quotient. There was no significant change in the tidal volume or the effective tidal air with smoking, or in the oxygen uptake, the CO_2 output or the per cent of oxygen extracted from the inspired air breathed, using the smoking device.

The blood gas measurements with step-up exercises before and after smoking two cigarettes were studied in 50 cases. The changes, after smoking, in the arterial blood oxygen saturation, in the CO_2 content in volumes per cent and in the minute ventilation (in liters per minute per square meter of body surface area) are correlated with the residual per cent of total lung capacity in Chart 2. The subjects smoked two cigarettes while in the sitting position following the first step-up exercise. A few had reactions, possibly related to the fasting state. These reactions consisted of feeling dizzy or weak, and a few subjects had headache, sweating and tachycardia. If the subject had a reaction following the smoking, a rest period of a few minutes was given and then the second exercise was started. In practically all cases, the subjects felt better after the exercise. A few of the subjects complained that the cigarette did not taste good. In none of the three

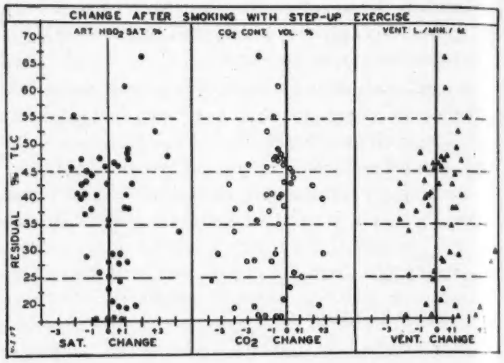

Chart 2.—Correlation of the residual per cent of total lung capacity with the change after smoking two cigarettes in the usual manner on the one minute step-up exercise measurements of: (1) Arterial blood oxygen saturation, (2) arterial CO_2 content and (3) the volume of pulmonary ventilation (liters per minute per square meter of body surface area). Measurements on 50 cases.

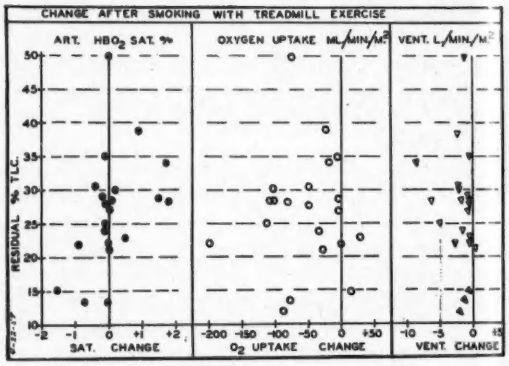

Chart 3.—Correlation of the residual per cent of total lung capacity with the change after smoking two cigarettes in the usual manner on treadmill exercise measurements of: (1) Arterial blood oxygen saturation, (2) oxygen uptake, and (3) the volume of pulmonary ventilation (liters per minute per square meter, body surface area). Measurements on 21 cases.

groups of subjects with varying degrees of emphysema was there significant change in the arterial blood oxygen saturation (Chart 2). Nor was there correlation between the change in arterial blood oxygen saturation after smoking and the residual per cent of total lung capacity. There was no significant change in the arterial CO_2 content and pH, before and after smoking with step-up exercise. The arterial pulse was consistently increased after smoking and the respiratory rate was increased slightly. A slight increase was noted in the average minute ventilation and oxygen uptake after smoking with step-up exercise. The data on individual subjects as to the CO_2 content change after smoking with step-up exercise revealed a tendency toward a decrease

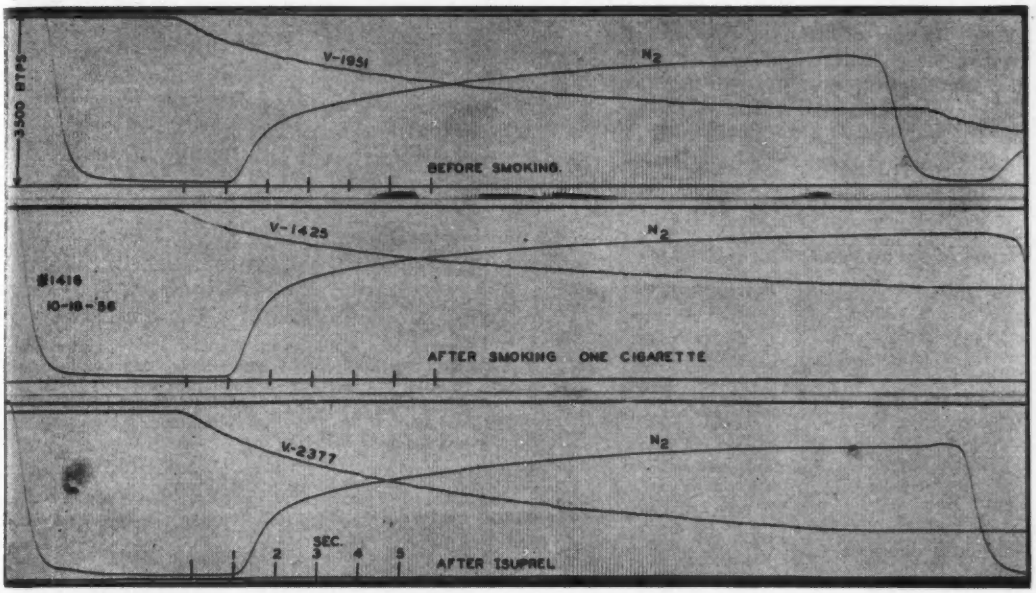

Chart 4.—The nitrogen curve (labeled N_2) and the corresponding volume (V) and flow during exhalation (total recorded as ml.) in a patient with severe emphysema, obtained by taking a single deep breath of oxygen and then blowing out as far as possible. The nitrogen was recorded from a nitrogen meter and the volume from the 13.5-liter Collins respirometer with a helipot to convert volume to electrical output. Impaired intrapulmonary mixing gives a prolonged sloping curve upward as shown in N_2 curve before smoking. After smoking the N_2 mixing curve was slightly improved (middle tracing) although the volume of the deep breath was reduced (vital capacity). After bronchodilator isuprel the vital capacity was significantly increased (V from 1425 to 2377 ml.) although the N_2 curve was not improved. Lung volume measurements are expressed at body temperature, pressure saturated (BTPS).

in CO_2. However, this was probably correlated with a slight increase noted in the minute ventilation (Chart 2). The average tidal volume was increased slightly after smoking.

Blood gas studies were obtained before and after smoking and treadmill exercise in 21 cases. The arterial blood oxygen saturation, the oxygen uptake in ml./min./M^2 BSA, and the ventilation as L./min./M^2 BSA are correlated with the residual per cent of total lung capacity for the 21 cases (Chart 3). There was no significant change in the arterial blood oxygen saturation after smoking. However, the oxygen uptake on exercise was decreased an average of from 565 to 516 ml./min./M^2 BSA after smoking. The standard deviation for the change in oxygen uptake on exercise was ± 53 ml. with a standard error of 11.5 ml. There was also an average ventilation change after smoking (Chart 3). The average minute ventilation was decreased from 13.05 to 11.62 L./min./M^2 BSA. The decrease in the oxygen uptake on exercise may be related in part to the decrease in the minute ventilation. However, no such decrease in minute ventilation was noted during step-up exercise after smoking two cigarettes. Direct tension measurements of arterial pO_2 and pCO_2 in the group of cases with treadmill exercises revealed no significant changes. The effective tidal air, computed on the basis of the expired pCO_2 and the arterial pCO_2, was not significantly changed in this group.

In several cases of severe emphysema, the single deep breath technique of oxygen with continuous recording of nitrogen on the nitrogen meter was employed and the volume of exhalation measured by electrical recording (Chart 4). No significant change in the air distribution as judged from the shape of the nitrogen curve was noted after smoking, even though the vital capacity usually showed some reduction. Although treatment with bronchodilator drugs after the smoking test increased the vital capacity significantly, the shape of the nitrogen curve was not improved.

In 41 subjects who smoked regularly the effect of one cigarette on pulmonary compliance was determined. The group consisted of eight normal persons and 33 patients with varying degrees of cardiorespiratory insufficiency as determined by complete pulmonary function studies. The pulmonary compliance was determined by a modification of the continuous cycling method, and timed pressure-volume loops were obtained over the range of quiet respiration. Pressure determinations were obtained by means of an esophageal balloon placed in the mid-esophagus. The resting compliance determina-

tion was obtained after the patient smoked a cigarette of his choice. There were no variations in the level of the balloon, the amount of air in the balloon or the position of the patient (variables that are known to affect the results in determining pulmonary compliance).

Vital capacity was also determined on most of the patients before and after smoking, utilizing the

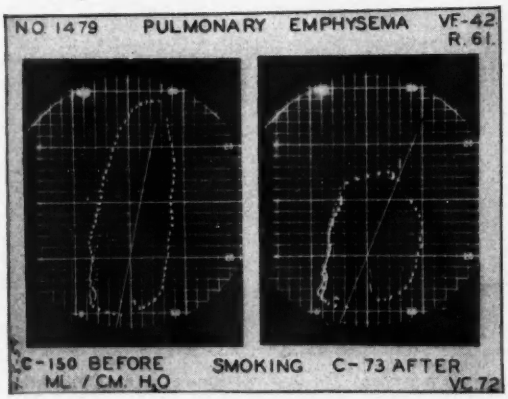

Chart 5(a).—Pulmonary compliance measurements before and after smoking one cigarette in the sitting position in a patient with severe emphysema (residual 61.0 per cent of total lung capacity (R), total vital capacity (VC) 72.0 per cent of normal, predicted and ventilation factor (VF) 42.0 per cent). Volume is recorded on the vertical axis and pressure on the horizontal axis. The interruption of the tracing permits timing, as the oscilloscope beam moves around counter clockwise, describing a complete loop for each respiratory cycle. The blip at the bottom is the no flow point at the end of expiration and the blip at the top the no flow point at the end of inspiration. The sloping line connects the points of no flow at the end of inspiration and expiration. Compliance (C) 150 ml./cm. H_2O before smoking and 73 ml/cm. H_2O after smoking.

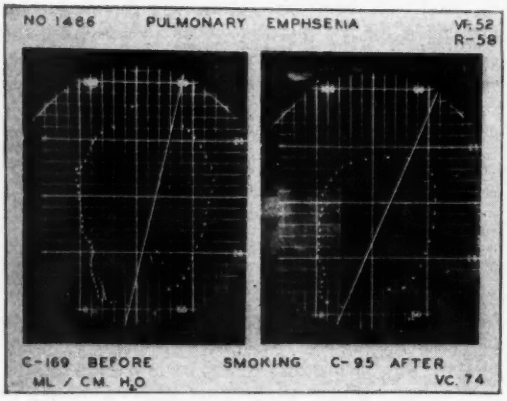

Chart 5(b).—Same as in Chart 5(a) except in a patient with a residual of 58.0 per cent of total lung capacity, total vital capacity 74.0 per cent of normal predicted and ventilation factor 52 per cent. Compliance 169 ml./cm. H_2O before smoking and 95 after.

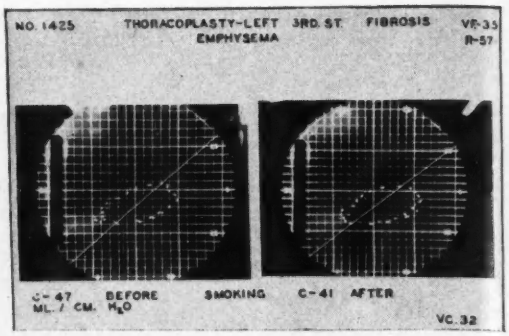

Chart 5(c).—Same as in Chart 5(a) except in a patient with fibrosis and emphysema and left thoracoplasty with a residual 57.0 per cent of total lung capacity, total vital capacity 32.0 per cent of normal predicted and a ventilation factor of 35 per cent. Compliance 47 ml./cm. H_2O before smoking and 41 after.

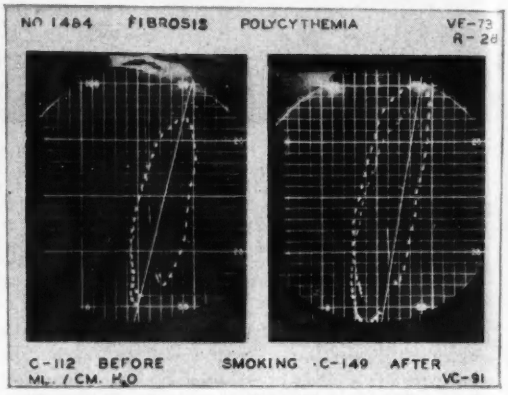

Chart 5(d).—Same as in Chart 5(a) except in a patient with fibrosis (x-ray) and polycythemia, with a residual of 28.0 per cent of total lung capacity, total vital capacity 91.0 per cent of normal predicted and ventilation factor 73.0 per cent. Compliance 112 ml./cm. H_2O before smoking and 149 after.

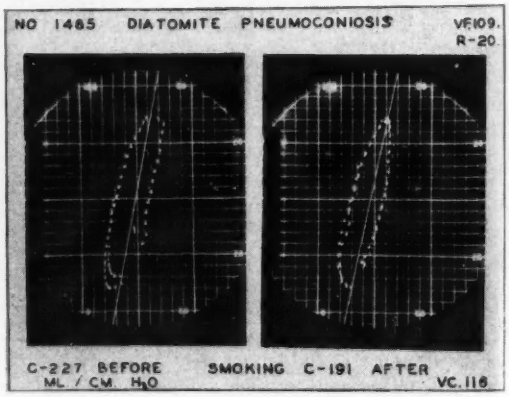

Chart 5(e).—Same as in Chart 5(a) except in a diatomite worker with a residual of 20.0 per cent of total lung capacity, total vital capacity 116.0 per cent of normal predicted and ventilation factor 109 per cent. Compliance 227 ml./cm. H_2O before smoking and 191 after.

TABLE 1.—*Effect of Cigarette Smoking on Pulmonary Compliance Measurements*

Case No.	Residual Per Cent of Total Lung Capacity	Ventilation Factor Per Cent	Resting Arterial pO_2 mm. Hg.	Sitting Vital Capacity		Compliance, ml./cm. H_2O		Elastic Work Breathing gm. M/liter of Ventilation	
				Per Cent Normal Predicted	Per Cent Change with Smoking	Observed	Change with Smoking	Observed Rest	Change with Smoking
1	61	42	75.6	73	— 5	1.0	— 73	45.00	+ 9.50
2	56	40	74.5	77	—16	83	— 22	57.50	+16.00
3	36	65	82.5	79	— 4	109	— 8	30.50	+21.50
4*	31	88	87.2	96	— 7	241	—131	17.50	+15.50
5	40	64	80.7	91	+ 1	169	— 15	27.50	+ 5.00
6	53	53	....	61	+ 8	163	— 26	32.00	+ 8.00
7	57	43	81.0	75	....	147	— 79	41.00	+13.50
8	35	64	92.1	41	—11	239	— 83	21.50	+ 5.50
9	23	100	97.5	92	—12	187	— 72	12.50	+ 7.50
10	48	55	87.3	60	....	48	+ 2	66.50	+12.50
11	43	69	81.8	95	....	96	— 11	43.00	0
12	67	61	85.6	60	....	179	....	18.00	— 5.00
13	62	32	....	54	....	153	— 50	15.50	+12.00
14	64	31	49.1	50	....	24	+ 3	12.00	— 1.50
15*	19	111	108.1	100	....	91	— 14	42.50	— 4.50
16	25	87	73.6	59	....	80	+ 24	38.50	—13.00
17	33	73	94.0	98	....	224	—109	16.50	+24.00
18	53	46	56.1	64	....	109	+ 56	22.00	— 3.50
19*	16	....	....	98	— 5	152	— 65	17.50	+19.50
20	57	44	63.0	30	—14	47	— 6	48.00	+ 5.00
21	....	....	....	95	— 2	143	— 57	28.50	+21.00
22*	18	114	90.2	116	— 1	297	— 28	8.00	— 2.00
23	59	31	66.4	62	—20	78	— 46	42.00	+10.50
24	48	55	91.3	83	+19	197	+ 19	27.50	— 5.00
25*	23	95	....	97	....	132	— 26	31.00	— 1.50
26	28	73	90.8	82	+ 4	115	+ 34	36.50	— 3.50
27*	20	109	102.0	110	— 3	239	— 49	23.50	+ 1.50
28	58	22	83.3	87	— 5	168	— 73	36.00	+18.00
29	29	71	....	67	+ 5	77	— 10	39.00	+ 1.50
30	....	....	....	63	+ 3	111	+ 25	45.00	—14.50
31	....	....	....	87	— 6	226	—108	23.50	0
32	32	72	....	102	....	267	— 56	21.50	— 5.50
33	66	29	59.9	66	— 8	77	— 15	34.50	— 7.00
34	31	86	88.5	80	+23	130	+ 44	18.00	+ 2.00
35	36	92	88.2	125	— 6	167	— 23	35.50	—10.50
36*	22	109	78.9	110	— 3	110	+ 21	38.00	— 7.50
37*	24	....	....	89	....	75	— 3	35.50	+ 9.00
38	....	....	....	75	— 5	111	— 6	50.50	0
39	44	66	....	86	—14	101	+ 1	86.50	— 7.50
40	68	32	75.6	29	—20	344	— 5	9.00	+ 2.00
41	24	89	84.6	92	+10	267	— 79	18.00	+23.50

*Normal subjects.

same volume recording apparatus with the patient in the sitting position. The elastic work of breathing was determined from the pressure-volume loop obtained at rest and again after smoking. Utilizing this method of determining pulmonary compliance in a group of normals, the mean pulmonary compliance was found to be 166 ml./cm. H_2O, with a range from 75 to 304 ml./cm. H_2O.

The results of the compliance studies shown in Table 1 and typical recordings are shown in Chart 5, a, b, c, d and e. There was a significant drop in pulmonary compliance in six of eight normal subjects in the study after smoking, with a mean decrease of 52 ml./cm. H_2O. In one subject no change was noted, while another had an increase of 21 ml./cm. H_2O. In the 33 patients with cardio-respiratory disease, 17 had a significant decrease in compliance after smoking. The maximum decrease was 109 ml./cm. H_2O with a mean of 57 ml./cm. H_2O. In ten patients no significant difference was noted between compliance while resting and while smoking. Six patients had a significant increase in compliance on smoking, with a maximum increase of 56 ml./cm. H_2O and a mean of 32 ml./cm. H_2O. There was no correlation of compliance change with the residual per cent of total lung capacity (Chart 6), as there were significant decreases in the group of normal subjects as well as in the emphysema group. On the whole, smoking tended to decrease compliance in the normal as well as in the emphysema group. The sitting vital capacity was decreased on an average 8.4 per cent in 20 cases after smoking one cigarette, and was increased 9.1 per cent in eight cases (Table 1).

The elastic work of breathing expressed, as gram meter per liter (gm. M/L) of ventilation, was de-

termined before and after smoking in the group of 41 subjects who were regular smokers. The eight normal subjects in the group had a mean value of 42.5 gm. M/L ventilation at rest. The 33 patients with cardio-respiratory impairment had a mean of 33.3 gm. M/L ventilation with a range from 9.0 gm. M/L ventilation to 86.5 gm. M/L ventilation. The values obtained for the elastic work of breathing by this method compare favorably with those reported elsewhere.[2,5,6,11,14]

After smoking, four of the normal subjects had an average increase of 15.0 gm. M/L ventilation in their elastic work of breathing while four had a decrease, the average for the group being 3.9 gm. M/L ventilation (Table 1 and Chart 7). In the group with cardio-respiratory impairment, 19 subjects had an increase, the average increase for the group being 11.5 gm. M/L ventilation. Eleven had a decrease, the average for the group being 6.95 gm. M/L ventilation. In three cases there was no change. The change in the elastic work of breathing after smoking was correlated with the residual per cent of total lung capacity (Chart 7). An increase in the elastic work of breathing after smoking was noted as often in the normal subjects as in those with severe emphysema. Similar changes were noted with regard to correlation with the ventilation factor. The elastic work of breathing is a static measurement, reflecting the elastic properties of the lung recorded at the instant of zero air-flow, and is therefore independent of time, but directly correlated to volume changes and rate of breathing. The elastic work of breathing was determined only at rest during normal tidal volume exchange.

No direct correlation was noted between the arterial pO_2 by direct tension measurements and changes in pulmonary compliance that were brought about by smoking. In 14 cases the arterial pO_2 after smoking showed a decrease; in four of them the compliance was increased, in two was unchanged and in eight was decreased (Table 1). In five subjects there was an increase in the arterial pO_2 after smoking; compliance was increased in two of them and decreased in three. In most of the subjects with a low compliance, there was a low arterial pO_2 also, although in some cases a low arterial pO_2 was associated with a normal compliance value.

There was a significant decrease in compliance after smoking in 56 per cent of the group, while 27 per cent showed no change and 17 per cent had an increase in compliance. Further studies of the effect of cigarette smoking on pulmonary compliance appear indicated in order to delineate the changes due to vascular effect, both in the greater and lesser circulation, and distinguish them from the direct effect on the respiratory mechanism.

In two cases follow-up studies of lung volume

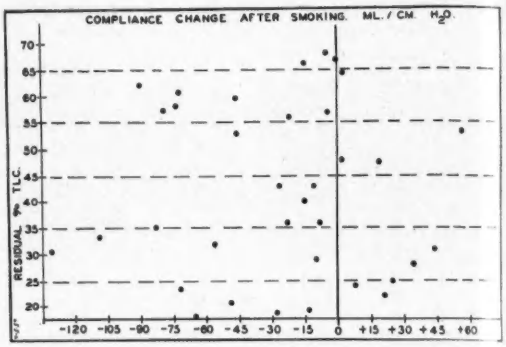

Chart 6.—Correlation of the residual per cent of total lung capacity with the change after smoking one cigarette in the usual manner on the pulmonary compliance measurement (milliliter volume change per centimeter H_2O pressure change). Pulmonary compliance change, ml./cm. H_2O, average mean —25, standard deviation ±39 and standard error 6.3.

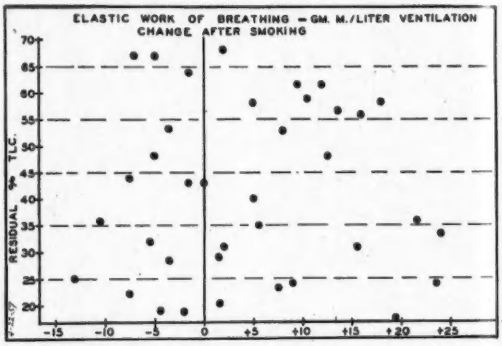

Chart 7.—Correlation of the residual per cent of total lung capacity with the change after smoking one cigarette in the usual manner on the elastic work of breathing (expressed as gram-meter per liter of ventilation).

were obtained after smoking of cigarettes had been stopped voluntarily by the subjects—for three months by one and two years by the other (Table 2). In both cases the residual air was decreased and the vital capacity increased after smoking was stopped. The timed vital capacity for three seconds and the maximal breathing capacity increased slightly in one case and decreased in the other. The subject in whom the decreases were shown complained of having had, for several weeks, a bad cold which had subsided very slowly. Bronchospasm was demonstrated in both cases before and after smoking was stopped (Table 2).

DISCUSSION

Loomis[10] carried out studies that led to a conclusion that there is a bronchoconstrictor factor other than nicotine in cigarette smoke. Bickerman and

TABLE 2.—*Lung Volume Changes After Cigarette Smoking Stopped*

Test	A Woman, Age 42 Years, Body Surface Area 1.67 Square Meters			A Man, Age 67 Years, Body Surface Area 1.90 Square Meters		
	Predicted	Observed June 25, 1953	Observed April 2, 1956*	Predicted	Observed Jan. 1, 1956	Observed March 12, 1957*
Total vital capacity, ml	3453	2540 (74%)	3320 (96%)	4165	2899 (70%)	3642 (87%)
Timed vital capacity, 3 sec. ml	3453	1650 (48%)	1929 (56%)	4165	1739 (42%)	1293 (31%)
Maximal breathing capacity, L./min.:						
Initial	104	26.2 (26%)	32.2 (31%)	121	35.0 (29%)	27.1 (23%)
After isuprel	104	48.0 (47%)	47.0 (46%)	121	51.0 (42%)	42.1 (35%)
Alveolar N_2, per cent	<1.5	6.89	5.05	<1.5	11.3	13.6
Residual air, ml	1190	2736 (227%)	2296 (193%)	1785	5263 (295%)	3382 (190%)
Total lung capacity, ml	4760	5276 (113%)	5616 (118%)	5960	8162 (137%)	7024 (118%)
Residual per cent of total lung capacity	25.0	51.9	40.9	30.0	64.5	48.1
Ventilation factor, per cent	100	41.0	49.0	100	39.0	39.0
Duration smoking stopped	.....	.....	2 years	.....	.....	3 months

*Study after smoking stopped.

Barach,[3] in a study of vital capacity and maximal breathing capacity in 122 subjects—91 with bronchial asthma and pulmonary emphysema and 21 normal persons—found no evidence of increased bronchospasm or impaired ventilatory function capacity in 108 of the subjects. There was a reduction of vital capacity and maximal breathing capacity in ten cases although unaccompanied by clinically perceptible increase in severity of asthma. An increase in vital capacity and maximal breathing capacity after smoking three cigarettes occurred in nine patients in whom coughing provoked by smoking resulted in expectoration of mucoid or mucopurulent sputum. A number of investigators have noted a decrease in vital capacity associated with long continued use of cigarettes.[4,16,18] Turley[17] noted no effect on vital capacity. Some of the observers who noted a decrease in vital capacity were of the opinion it may be associated with bronchospasm as a result of smoking, but the individual responses were quite varied. In some instances even an increase was noted. The decrease noted in pulmonary ventilation in some patients after smoking has been explained on a basis of the expectoration of mucopurulent secretions.[3] In some patients carbon monoxide may be a factor in stimulating pulmonary ventilation with smoking. However, Asmussen and Chiodi[1] carried out a study in which it was noted that the pulmonary ventilation was not stimulated by carbon monoxide poisoning as it was in hypoxemia due to breathing a low oxygen mixture.

The problem of allergic sensitivity to tobacco smoke has to be considered in studies like the present one. Some investigators regard allergic reaction to cigarettes as rather infrequent, although there can be little question that smoking or exposure to smoke from tobacco can aggravate asthma in some persons. The number of reported cases with detailed evidence of sensitivity to tobacco as a cause of respiratory manifestations is surprisingly small in view of the widely quoted statement that in one per cent of patients with asthma, tobacco is a factor.[19]

In a review of the literature very little information was found on changes in the blood associated with smoking, and not much more on gas exchange; what there was of the latter was principally on resting oxygen uptake. In the present study, when cigarette smoke was inhaled with the smoking device, there was a significant lowering in the resting arterial blood oxygen saturation in the majority of patients who had severe or very severe pulmonary emphysema. Direct tension measurements of arterial pO_2, using the bubble technique of Riley, also demonstrated a significant decrease in this group of subjects. However, the average pCO_2 was increased slightly but not to a statistically significant degree. There was no significant change in the ventilation volumes at rest when tests using the smoking device were carried out. Tests that were done in 50 cases before and immediately after smoking, with step-up exercise, showed no consistent significant changes in the blood gas exchange. Studies of 21 subjects before and after smoking, with treadmill exercise, did show a significant decrease in the exercise oxygen uptake after smoking. However, there was also a significant decrease in the minute ventilation, and this may have been the cause of the reduced oxygen uptake on exercise. One has to consider, however, that the reduced exercise oxygen uptake may possibly reflect some change in pulmonary vascular resistance, which could result from an increase in pulmonary blood volume or from bronchospasm.

When a very sensitive test such as pulmonary compliance was employed, significant changes in the pressure volume relationship were obtained in subjects who were essentially normal and also in those with various degrees of pulmonary insufficiency. When the elastic work of breathing was calculated, it was noted that smoking increased the work of

breathing in most subjects. There was no significant correlation of the change noted in compliance with smoking and the severity of the pulmonary emphysema or fibrosis.

In practically every case of severe emphysema which has been studied in this laboratory, when there was no other apparent cause for emphysema, there was a history of heavy cigarette smoking for many years. Significant changes in the arterial blood oxygen saturation were found only in the subjects with severe or very severe pulmonary emphysema when they inhaled the smoke with the smoking device, which delivered smoke in greater concentrations than was obtained by ordinary cigarette smoking. The experiment with the smoking apparatus was designed to try to intensify the effects of smoking as far as possible to see if blood gas exchange could be affected.

The data of this study in general indicated that patients with severe emphysema would be better off if they stopped smoking. No apparent difference was noted regarding the brand of cigarette smoked, or the presence of the filter tip. In normal persons the pulmonary compliance changes in some subjects were the only constant abnormality noted; this may be an undesirable change and may be a factor producing changes later on in some but not in all subjects, with respect to the development of a significant degree of emphysema.

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Social Security Footnotes

THE "SOUNDNESS" of Social Security depends on compulsion, high employment, and no wars.

—From the Department of Public Relations, American Medical Association

Emergency Operations in the Newborn

DAVID B. SHELDON, *M.D.*, Los Angeles

• **With the present-day development and understanding of anesthetic methods, fluid and electrolyte therapy, antibiotic medications and pediatric care, many congenital anomalies once uniformly fatal are now being successfully treated by emergency operations in the neonatal period. The eight most common of these which demand emergency operation in the immediate postnatal period are esophageal atresia and tracheoesophageal fistula, diaphragmatic hernia with dislocation of the abdominal viscera into the chest, malrotation of the intestine with obstruction, intestinal atresia, meconium ileus, imperforate anus, omphalocele and myelomeningocele.**

Although infants born with any of these serious problems often are born prematurely and often have more than one congenital anomaly, survival rates in the surgical treatment of these conditions are steadily improving. Early diagnosis and prompt treatment are the most important factors in the continued improvement of these survival rates.

FIVE OF THE SEVEN commonest congenital anomalies which demand emergency operations in the newborn are varieties of obstruction to the gastrointestinal tract. The other two are varieties of herniation. When successfully treated, most of the infants with these anomalies can be given an entirely normal life.

These seven relatively common congenital anomalies are: Esophageal atresia, diaphragmatic hernia, malrotation of the intestine, intestinal atresia, meconium ileus, imperforate anus and omphalocele. There are other less common conditions which demand immediate operation in the newborn such as intestinal obstruction due to an annular pancreas, but this discussion will concern only the more frequently encountered entities.

A significantly high proportion of infants born with one of these congenital anomalies will be born prematurely and also a considerable number will have more than one congenital malformation. The mortality rate in these cases bears a direct relation to the degree of immaturity and to the presence of other congenital anomalies.

Infants seem to tolerate operation in the immediate newborn period better than a few days later. One of the reasons for this is that with the passage of time the effects of the congenital anomaly become manifest. Aspiration, atelectasis and pneumonia occur, and distention, vomiting, dehydration and electrolyte depletion become established. These factors not only complicate the surgical procedure but endanger the postoperative course of the infant. In all of the anomalies mentioned, there is a direct increase in the mortality rate with increasing age of the infant. However, once the complications of the anomaly have become established, time must be invested preoperatively in attempting to overcome as many of the existing physiological derangements as possible.

The anesthesia used in these tiny patients is fully as important as the operation. A highly trained and experienced anesthesiologist is needed. Thought should be given to the selection of an agent which allows good oxygenation, does not stimulate the secretion of mucus in the respiratory tract and is rapidly eliminated. In most cases the necessary procedures can be accomplished with a relatively light anesthesia, since relaxation in an infant is seldom a problem. Cyclopropane is the agent most often nearly ideal in these cases. Endotrachael intubation is frequently necessary and special care must be used in this regard since injury to the tiny larynx may lead to a fatal laryngeal edema after operation. Special pediatric anesthesia equipment is often necessary.

The administration of fluids and blood to the newborn infant requires fine judgment. Certainly, blood lost during a surgical procedure must be accurately measured and replaced. To accomplish this an intravenous polyethylene cut-down catheter is inserted at the beginning of operation. Newborn infants are generally well hydrated. They will tolerate a surprising amount of dehydration without trouble. If there are no abnormal fluid losses they can easily go 48 hours or more without additional fluid. However, their tolerance to excessive fluid administration, particularly in the form of saline solution, is very limited indeed. The cardiovascular and renal systems are not mature at birth and thus do not allow the wide latitude permissible in the fluid therapy of adult patients. Pulmonary edema is a constant danger in the immature lungs of an infant who has received only a slight excess of saline solution. By keeping these tiny patients on the "dry side" more of them will be brought successfully through

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the surgical procedures necessary to correct their congenital anomalies.

The surface area of an infant is relatively greater in proportion to his weight than an adult's, and heat loss during the operative procedure may become a serious problem. Efforts should be made to conserve the baby's heat and maintain his normal temperature during and after operation.

Frequently respiratory complications prove to be the limiting factor in the treatment of newborns. Every effort should be made to avoid aspiration, atelectasis and respiratory infections in these infants, who often have imperfectly expanded lungs to begin with, and frequently have underdeveloped protective cough reflexes. The tiny bronchial tubes of a newborn easily become blocked with plugs of dried mucus. A humidified atmosphere rich in oxygen is a great help in preventing this complication. Antibiotics are necessary to combat these respiratory complications.

Vitamin K must often be given to counteract the hemorrhagic tendencies found in the newborn. Nasogastric suction through a multi-holed fine catheter is necessary to help alleviate the distention of intestinal obstruction and to permit the bowel to rest postoperatively until normal function resumes.

Space does not permit the giving of credit to all the surgical pioneers who developed the successful methods of handling the surgical correction of congenital anomalies in the newborn. However, no discussion of this subject is complete without mentioning the contributions of Ladd and Gross and the group at the Boston Childrens' Hospital in compiling a monograph which serves as a guide for less experienced surgeons facing these relatively infrequent cases in the community.

Each of the more common congenital anomalies requiring emergency operation in the newborn will now be considered separately.

Esophageal Atresia

Esophageal atresia with a tracheoesophageal fistula occurs not infrequently. Over 90 per cent of these malformations have a blind proximal esophageal pouch and a communication between the distal esophagus and the trachea at the posterior aspect of its bifurcation.

With prompt diagnosis and treatment, a large percentage of infants with this condition can be saved. The early symptoms are excessive salivation, coughing and gagging during attempted feeding, quantitative regurgitation of food, and increasing respiratory distress, with bouts of cyanosis as the infant aspirates food or salivary secretions. The diagnosis may be confirmed by attempting to pass a small soft rubber catheter gently down the esophagus and meeting an obstruction, or by x-ray studies with a small amount of iodized oil introduced into the esophagus to demonstrate the blind proximal pouch. Air seen in the stomach and intestinal tract indicates the presence of a communication between the trachea and the distal esophageal remnant. These films will also demonstrate the degree of atelectasis and aspiration pneumonia usually present in these infants unless the diagnosis has been made in the very early hours of life. Barium should not be used in making these studies, since it is irritating when aspirated and will further severely complicate the already precarious pulmonary situation.

Approximately one-third of the infants born with esophageal atresia will have other congenital anomalies which often are an additional serious threat to their lives. Nearly one-fifth of these babies will be premature.

Once the diagnosis has been made, constant esophageal suction should be instituted to prevent the further aspiration of salivary secretions. The infant should be placed in a warm, moist, oxygen-rich atmosphere. Chemotherapy should be started to combat the respiratory complications, and parenteral fluids should be given as deemed necessary. Preparations for the definitive surgical repair of this anomaly should be begun at once.

In most infants with this problem, a single stage closure of the tracheoesophageal fistula and an end-to-end anastomosis of the divided esophageal segments can be done. The right side of the chest is opened through the fourth intercostal space, the mediastinal pleura is incised and the azygos vein is ligated and divided, exposing the retrotracheal region. The distal esophagus is freed and followed up to its connection with the posterior surface of the carina, where it is divided and sutured. The distal esophagus may be gently dilated so that it approximates the size of the proximal pouch. Considerable freeing of the distal segment may be necessary in order to achieve an anastomosis without tension. The proximal pouch is identified at the apex of the chest and gently freed from its attachment to the posterior wall of the trachea. An opening is made in this pouch and an anastomosis between the two freed ends of the esophagus is made, using two layers of fine interrupted silk sutures. Once the anastomosis is completed, the mediastinal pleura is closed loosely, then the chest wound is closed in layers, and a catheter is left in place for postoperative suction. Frequently it will be found wise to perform gastrostomy immediately following the primary esophageal anastomosis so that feeding of the infant may be begun before the esophageal anastomosis has safely healed.

After operation constant nursing care is necessary, with particular attention to frequent oro-

pharyngeal suction to prevent further aspiration and pneumonia. In the cases in which the distance between the proximal and distal portions of the esophagus is too great to perform a primary anastomosis without tension, the right leaf of the diaphragm may be opened and the stomach freed so as to bring it up into the chest and thus gain additional length for an anastomosis. In some situations, even this may not suffice and it is necessary to close the tracheoesophageal fistula if one exists, create a cervical esophagostomy with the proximal segment so that the oropharyngeal secretions will not be aspirated but will leak out onto the neck of the patient, and then establish a feeding gastrostomy. When these measures have been carried out, the baby is encouraged to grow and at some later date a multiple-stage esophageal reconstruction is done.

The mortality rate bears a direct relation to the degree of prematurity, the presence of other serious congenital abnormalities and the condition of the infant before operation. This latter is directly related to the length of time between birth and the recognition of the congenital abnormality. Most of these infants who die do so of the pulmonary complications secondary to the aspiration of food and salivary secretions; but with prompt diagnosis and treatment more than half of them should survive.

Diaphragmatic Hernia

Diaphragmatic hernia in the newborn occurs most frequently in the left posterolateral region of the diaphragm. It is the result of failure of fusion of the pleuroperitoneal sinus or foramen of Bochdalek. Most infants with this abnormality will die promptly unless treated, because of the compression of their lungs by the abdominal viscera in the chest. The lives of most infants with this congenital abnormality can be saved by prompt surgical intervention. Although congenital hernia of the diaphragm may appear in other locations—the retrosternal area, esophageal hiatus, or the right posterolateral foramen—by far the vast majority of them occur in the left posterolateral region. Most of these defects do not have a hernial sac. The pleural cavity on the defective side is filled with abdominal viscera and the lung on that side is completely collapsed, the mediastinum shifted and the vital capacity of the infant seriously impaired.

The symptoms associated with these diaphragmatic hernias are cyanosis, dyspnea and vomiting. Some infants are able to tolerate such hernias with a remarkable lack of symptoms. Breath sounds will be absent on the affected side and will be replaced by peristaltic sounds. After birth, the infant swallows air, inflating the intestinal loops located in the chest. This further compresses the lung, shifts the mediastinum and aggravates the already seriously diminished vital capacity. The symptoms may be delayed in onset and progressive in severity. Prompt diagnosis and treatment are necessary for successful outcome. The inflated loops of bowel not only further reduce the vital capacity but complicate the problem of replacement of the bowel into the abdominal cavity which may be already too small to accommodate the structures which normally should be there. X-ray examination will disclose the presence of gas-filled loops of bowel high in the chest, complete collapse of the lung on that side, shift of the mediastinum and partial compression of the lung on the opposite side.

In most cases the abdominal approach for the repair of this hernia is preferable because a significant percentage of the infants will not have proper rotation of the intestine, and this difficulty can be remedied at the time the diaphragmatic hernia is repaired. Furthermore, if there is pronounced disparity between the size of the abdominal cavity after repair of the hernia and the number of loops of bowel which must be accommodated within this cavity, a repair similar to that used for a large omphalocele may be employed.

Through a long left paramedian incision the abdominal cavity is entered, the remaining viscera are gently retracted and the loops of bowel extending up into the chest through the hernial opening are gently drawn down into the abdominal cavity. It may be necessary to insert a catheter along the course of these bowel loops to release the "vacuum" in the pleural space and facilitate the withdrawal of the bowel and viscera. With the bowel removed from the pleural cavity the hernial opening may be closed, imbricating the edges of the diaphragm, if possible. It is necessary to secure expansion of the lung as this closure proceeds, and this requires the use of endotracheal anesthesia with judicious positive pressure by the anesthetist during this phase of the repair, and the placement of a chest catheter for postoperative suction. Without the use of an endotracheal tube the positive pressure efforts on the part of the anesthetist will suffice only to inflate the stomach and further complicate the reduction of the hernia. The viscera are then replaced carefully within the peritoneal cavity and the abdominal wound closed meticulously in layers. Even though the abdominal cavity may not have been fully developed, it is generally possible to enclose all the abdominal viscera with a normal repair. However, on occasion it may be necessary to close only the peritoneum and skin, leaving the definitive abdominal closure for a second stage. Attention must be paid postoperatively to the lung to see that it remains fully expanded.

With prompt recognition of this condition and

prompt treatment, fully 90 per cent of these infants should be successfully treated. In choosing the anesthesia for this procedure, one must keep in mind the necessity of delivering a high concentration of oxygen owing to the respiratory embarrassment of the infants. Occasionally the diaphragm on one side may be almost completely absent or the defect may be so large that the edges cannot be brought together. In such cases the ingenuity of the surgeon is severely taxed in efforts to raise flaps of peritoneum and pleura to bridge over the defect.

Malrotation of the Intestines

Malrotation of the intestines and colon is a condition which occurs not infrequently in the development of the fetus. Normally during embryologic development, the midgut develops at a rate faster than the capacity of the abdominal cavity. Thus one finds portions of the alimentary tract protruding into the base of the umbilical cord. As the peritoneal cavity grows, the midgut retracts into the abdominal cavity and a form of rotation occurs which drapes the colon around three sides of the abdominal cavity and gives the intestinal mesentery a line of attachment extending roughly from the ligament of Treitz to the ileocecal region. Normally the ascending colon and the descending colon are adherent to the lateral abdominal walls. This rotation and fusion process may become arrested or fail of completion. With incomplete rotation, one frequently finds a mobile cecum situated just below the antrum of the stomach. Obstruction to the second or descending portion of the duodenum occurs from bands of peritoneum that extend from the malpositioned cecum across in front of the duodenum to the abdominal wall. The cecum itself may rest just anterior to this portion of the duodenum and compress it. When this developmental abnormality is present, the entire small bowel has only a rudimentary attachment to the posterior abdominal wall, and instead of there being a line of fixation for the small bowel mesentery, there is only a single point of fixation at the aortic origin of the superior mesenteric artery. The entire small bowel may easily twist about this single point of fixation.

In approximately one half of patients with malrotation of the intestines and colon, there is an associated volvulus of the midgut. This volvulus usually occurs in a clockwise direction, and may be several complete turns. Such a volvulus not only obstructs the lumen of the bowel but may infarct the entire midgut by occlusion of the superior mesenteric vessels. Thus two pathologic entities may arise from one congenital abnormality: (1) Compression and obstruction of the second portion of the duodenum due to bands from the malposition of the ileocecal region across the descending portion of the duodenum, and (2) volvulus of the midgut with infarction and obstruction.

Although in the majority of infants with this congenital abnormality, signs and symptoms develop early in life, occasionally difficulties do not occur until a later age. The signs and symptoms are vomiting and abdominal distention usually confined to the upper abdomen because it is only the stomach and first portion of the duodenum that are dilated. Dehydration and electrolyte imbalance follow rapidly. This condition is sometimes difficult to differentiate from duodenal atresia. However, immediate surgical treatment is required for both. X-ray examination will disclose a greatly dilated stomach and there often is seen a single bubble of gas in the first portion of the duodenum. The remainder of the intestinal tract is usually empty, although a few scattered bubbles of gas may occasionally be seen. A barium enema is often useful and will reveal the incomplete rotation of the large bowel. Barium should not be given from above, since it rarely adds much to the diagnosis and will tend to obstruct the bowel postoperatively.

Treatment of this condition consists of careful rehydration and replacement to overcome electrolyte deficiency, aspiration and decompression of the proximal bowel and stomach, and early surgical intervention. Early operation should be stressed because of the danger of midgut infarction when volvulus is present. Sometimes when the abdomen is opened, the only viscera visible are multiple loops of dilated small bowel. The situation may be clarified if the surgeon will gently deliver the entire intestinal mass out onto the abdominal wall. Once this has been accomplished, the twisted midgut mesentery may be seen and the intestinal mass properly unrotated. With the release of the constriction of the superior mesenteric vessels, normal color should soon reappear in the intestinal loops unless irreversible changes have already occurred. The bands between the right parietal peritoneum and the cecum which are obstructing the second portion of the duodenum must be released, allowing the entire colon to move into the left side of the abdomen. Once it has been determined that the midgut is viable, the abdomen is closed.

After operation, gastric suction is maintained constantly until the patient has recovered from the ileus that accompanies this condition and the operative treatment. About 80 per cent of the patients treated for malrotation of the colon and intestines with duodenal obstruction should survive, whereas only about half that number who also have volvulus of the midgut will survive. Surely the sooner the diagnosis can be made, and the sooner proper surgical treatment can be carried out, the greater will be the survival rates in both groups.

Intestinal Atresia

Intestinal atresia is not common. It may be difficult to diagnose, and delay is usually associated with severe deterioration of the baby's condition. The atritic segment of bowel may be short or long and may occur anywhere, but most frequently is found in the duodenum or in the ileum. The symptoms are vomiting with progression in frequency and intensity. No cornified epithelial cells can be found upon microscopic examination of the stool (Farber's test). Extensive abdominal distension may or may not appear, depending upon where the atresia is located; however, usually the upper abdomen in the region of the stomach will become bloated intermittently. The signs and symptoms of dehydration and toxicity become progressively superimposed upon the symptoms of intestinal obstruction. Abdominal x-ray films show a greatly dilated intestinal tract proximal to the obstruction, with no bowel gas beyond it. No contrast medium should be used. Barium will effectively block any anastomosis subsequently achieved. Every effort should be made to decompress the stomach with a small urethral catheter before operation. Often the infants will need a period of fluid and electrolyte replacement before they are operated upon.

The problem at operation is to achieve a satisfactory anastomosis between the dilated segment of bowel proximal to the atresia and the tiny underdeveloped bowel distal to the block. When the atresia is in the duodenum or jejunum, every effort should be made to secure a side-to-side anastomosis, bypassing the blocked segment. When the atresia is in the terminal ileum or colon, a Mikulicz exteriorization procedure can be carried out, bringing out—sewn together—the dilated proximal loop and the collapsed distal loop. The spur between these is subsequently crushed and eventually the enterostomy stoma is closed. The problems presented by this method of treatment are those of continued severe depletion of fluid and electrolytes by loss through the ileostomy stoma. A primary anastomosis is the treatment of choice whenever possible.

After operation, considerable patience and care are necessary before the undilated distal bowel begins to accept thin fluid feedings through the anastomosis from above.

This congenital anomaly is difficult to treat successfully, but a survival rate of better than 50 per cent has been achieved.

Meconium Ileus

Meconium ileus causing intestinal obstruction in the newborn is also an extremely difficult condition to treat successfully. This is because the meconium ileus is only a symptom of a widespread generalized disease, characterized by failure of the mucus-secreting glands of the respiratory and gastrointestinal systems to function properly as well as failure of the pancreas to form its digestive enzymes.

In infants with this disease the symptoms may be those of intestinal obstruction which may be difficult to distinguish from any other form of neonatal intestinal obstruction. Frequently the babies have become distended and severely depleted by the time operation is undertaken. At exploration, distended loops of bowel are found proximal to the obstructed segment, which contains a very thick tenacious inspissated plug of meconium. The obstruction may extend for some length and there may be more than one. That there are different surgical maneuvers recommended for the treatment of meconium ileus indicates that no single method is entirely satisfactory. A resection and anastomosis of the obstructed segment of bowel seems to offer the best chance to the infant if the obstruction is high in the small bowel. If the obstruction is in the terminal portion of the ileum, where it often is, this segment can be exteriorized and resected, forming a double ileostomy by use of the Mikulicz technique. A crushing clamp is applied later to the spur between the two loops of bowel, permitting the intestinal contents to pass on into the distal bowel. The ileostomy stoma is later closed. The disadvantages of this technique are those of the tremendous problems presented by uncontrolled fluid and electrolyte losses from the ileostomy. The more proximal the ileostomy, the more severe these problems. The advantages are that it is quick, aseptic and may be the only procedure that an already severely ill child could possibly survive.

Many of the patients die sooner or later of the pulmonary complications of generalized mucoviscidosis, despite the alleviation of intestinal obstruction.

Imperforate Anus

Imperforate anus is probably the most frequent congenital anomaly requiring emergency operation in the newborn. It occurs in several forms, varying from mild anal stenosis to a blind rectal pouch ending high in the pelvis. The majority of cases are of the latter type. Three fourths of the infants will have a fistula connecting the blind rectal pouch to the bladder, urethra or perineum in the males, or to the vagina or perineum in the females.

In most cases the symptoms of intestinal obstruction develop shortly after birth—first obstipation, abdominal distention and vomiting and then dehydration and manifestations of the toxic effects of intestinal obstruction soon afterward. If there is an associated fistula of sufficient size, the infants may pass meconium and gas through the urinary tract or from the vagina. Occasionally a perineal fistula

is large enough size to permit bowel function so nearly normal that the rectal abnormality is not discovered until the patient is in an older age group.

X-ray studies are helpful in determining the level of the atresia. If the child is held inverted, a plain abdominal film will show gas rising to the distal end of the colon; and by placing a lead marker on the perineal skin, the distance between the blind pouch and the surface can be determined. For these studies to be significant the child must have passed enough gas through the length of the intestinal tract to outline the blind end of the colon.

The treatment chosen for this condition depends upon the anatomical type of the anomaly. In cases of anal stenosis, repeated and gradually increasing dilatation usually solves the problem. If there is only a thin membrane obstructing the anus, a simple perineal excision of this membrane followed by serial dilatations is usually all that is necessary. In the most common type, in which the rectum ends in a blind pouch high in the pelvis (an inch or more from the anal skin), two types of treatment must be considered. First, a simple sigmoid colostomy may be performed and the definitive reconstruction of the anal canal deferred. This is the procedure of choice when the infant is premature, or when its condition is precarious due to the intestinal obstruction, distention and dehydration. Care must be taken in doing the colostomy to leave ample distal bowel for the subsequent pull-through procedure.

Second, in ideal cases—those in which the diagnosis has been made early and the infant was delivered at full term and in good condition—a combined single stage abdominal-perineal reconstruction of the rectal canal can be carried out. Through an abdominal approach the rectal pouch is freed, any existing fistulas are identified and closed, and dissection is carried down through the pelvis as far as is practicable from above. A catheter in the urethra in the male or a finger in the vagina in the female will aid in this dissection. Then the perineal approach is begun by incising vertically in the midline, dividing the sphincter, which can be identified by stimulation, and carrying the dissection up into the pelvis between the levator ani muscles. Once the pelvic cavity is entered, the rectal pouch is drawn down through the passage, the perineal structures are reconstituted and the bowel is anchored to the subcutaneous tissues with interrupted sutures. It is then opened and the mucosa sutured to the edges of the skin, care being taken to bring the bowel through the center of the anal muscular ring, which is reformed. When a fistula involves the urinary tract in males, a suprapubic cystostomy catheter is left in place.

Although a blind rectal pouch which approaches closely to the perineal skin can frequently be mobilized from below sufficiently to complete the operation by the perineal route alone, it is inadvisable to attempt this approach initially if the distance between the perineal skin and the pouch is over three-quarters of an inch. It is also advisable to err on the side of conservatism in performing a preliminary colostomy, since, all other considerations being equal, the mortality rate with the extensive one-stage pull-through operation in newborn infants tends to be higher than with the two-stage repair.

With proper selection of the procedure and prompt treatment, 90 per cent of the infants should survive.

Omphalocele

Omphalocele is a herniation of the abdominal viscera into a sac at the base of the umbilical cord covered only by a fused layer of peritoneum and amniotic membrane. This condition is not common. It is thought to arise from a disparity in the relative rates of development of the size of the abdominal cavity and the volume of the developing intestinal and abdominal viscera. Normally before birth the abdominal cavity has assumed a size that will accommodate all the viscera, and the anterior abdominal wall closes, leaving only a narrow channel in the umbilical cord. The diagnosis of this condition is at once evident upon the birth of the baby. The omphalocele may be very large and may contain nearly all the abdominal viscera, including the liver. The stump of the umbilical cord will be attached to the apex of the sac. This condition is one of surgical emergency in the newborn, since the membranes rapidly become dried and brittle and rupture, evisceration and peritonitis ensuing. Also, there is a very low bacterial resistance in these membranes. Other associated congenital abnormalities occur in these infants with a frequency considerably more than statistically expected. Another factor dictating promptness in repair of this abnormality is the fact that as time passes the intestinal tract becomes inflated, which further complicates the reduction of the abdominal contents into the already too small abdominal cavity. Before the era of antibiotics and chemotherapy, rupture of this sac was uniformly fatal.

The repair of omphaloceles may be performed by a single or two-stage procedure, depending upon the size of the sac and defect. When the viscera can be easily replaced within the abdomen without undue pressure and the abdominal wall closed meticulously in layers without tension, this is the procedure of choice. However, when the intestines are inflated or the abdominal cavity is unduly underdeveloped, compressing the viscera back into this cavity may force the diaphragms up and give rise to serious embarrassment of the vital capacity. The vena cava

may be compressed, diminishing the return of blood to the heart, and the intestines themselves may be so squeezed as to seriously delay or embarrass the gastrointestinal functions of the infant. In these cases it is far wiser to use the two-stage repair.

Basically, the technique of the two-stage repair of an omphalocele consists of leaving the fused peritoneal and amniotic sac intact, undermining skin flaps widely on either side and bringing them together over the sac, which has been previously thoroughly cleaned. Such a repair leaves the infant with a large, skin-covered ventral hernia; however, at a second stage, once the abdominal cavity has grown large enough to accommodate all the viscera without embarrassing the child's respiration, the ventral hernia may be converted into a normal abdominal contour. Approximately two-thirds of the infants with this defect should survive. There is a direct relationship between the size of the omphalocele and the mortality rate.

A myelomeningocele is a similar problem which may require emergency operation in the newborn, but a discussion of this anomaly rightly belongs in the field of neurosurgery.

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Black Lesions of the Skin

S. WILLIAM BECKER, M.D., Long Beach

• **Benign melanocytic lesions include lentigo, ephelid (freckle), pigmented nevus, sacral spot, blue nevus, and combined nevus and blue nevus.**

Malignant melanocytic lesions are melanomas, which arise from melanocytes at the epidermodermal junction, or, rarely, from blue nevi. They usually originate in brown plaques known as lentigo maligna, in pigmented nevi, or in normal skin.

Melanoma is diagnosed clinically in less than 50 per cent of instances. Biopsy is therefore of great importance, since practically all melanoma can be cured by adequate early resection.

IN CONTRAST to the sometimes gaudily pigmented lower animals, man appears rather drab. The six pigment systems recognized by Weidenreich[28] in the lower forms—pericoelomic, perivascular, perineural, ocular, dermal, and epidermal—have been reduced in man to:

Perineural—a rather primitive occurrence of melanocytes in the pia mater about the medulla;

Ocular—prominent;

Epidermal—prominent in the dark races, less conspicuous in Caucasians;

Dermal—sacral spots and blue nevi.

The pericoelomic and perivascular systems are recognized in man only as the probable source of melanomas that occasionally originate (or seem to) in the inner organs, and which can be understood only as atavistic phenomena.

Other sources of skin color—hemosiderin, carbon and certain metals—are rare and will not be discussed in this presentation.

The pigment-forming cells, formerly called melanoblasts ("pigment-formers"—Bloch and others), are designated melanocytes, according to the classification of Harvey, Dawson and Innes,[12] adopted by interested participants at the Second Pigment Cell Conference.[24] Primitive (stem) cells are called "melanoblasts," the differentiated cells which form melanin "melanocytes," and the dermal phagocytic melanin-containing cells "melanophages." The dendritic cells in amphibians in which the melanin granules gather and scatter, depending on circumstances, are called "melanophores," a term preferred by most zoologists.

Zimmerman and Becker,[30] by study of human embryos and fetuses (chiefly Negro), observed that pigment-forming cells appear in the dermis first as a single layer of argyrophil cells. This single layer later becomes double and the cells of the more superficial layer migrate to the epidermodermal junction, where they become permanently located between or just proximal to the basal cells. The cells of the deeper layer remain in the deeper dermis.

The cells of the superficial layer become dioxyphenylalanine-positive as they are attached to the epidermis. They become tyrosine-positive after exposure to the skin of a ferment activator, such as ultraviolet irradiation, alpha, beta or gamma rays. In sections of unirradiated fixed and stained skin, the cells may be seen clinging to the proximal margins of the palisade basal cells or scattered regularly between these cells. Unlike the epithelial cells, they have no intercellular bridges, probably because of shrinkage of their somewhat basophilic cytoplasm, they appear as though situated in clear spaces; hence were called "clear cells" by Masson.[16] Under the influence of activating irradiation, the cells enlarge and alter their shape in the form of dendrites, which extend outward between the basal cells. Melanin granules appear on mitochondria[29] within the cell body and in the branches, which end in cup-shaped termini that appear to cover as an umbrella the distal pole of the nucleus of the basal cells (nuclear caps).[2] The melanocytes function in pigmentation of the skin under the influence of the sunburn spectrum of ultraviolet irradiation and of alpha, beta and gamma rays. They also become hyperpigmented in lentigo and ephelid (freckle).

Melanocytes also have the faculty of multiplying. If the neoplasia is benign, a pigmented or nonpigmented melanocytic nevus (pigmented nevus) results; if malignant, malignant melanoma is produced, pigmented or nonpigmented.

Loss of pigment-forming function of the melanocytes results in various types of leukoderma, including vitiligo.

The deeper layer of pigment-forming cells is the origin of sacral spots, blue nevi (including the progressive blue nevus) and, rarely, of malignant melanoma. Most of the cells of this layer begin to

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disappear at or before birth, and continue to do so for several years.

In amphibians, fowl and mice, melanoblasts and melanocytes have been traced back to the neural crest. This origin has not been demonstrated in human beings, for obvious reasons, but the resemblance of pigment-forming cells in human beings to nerve cells is manifest in many observations: The presence of argyrophil cells in fetuses; staining by nerve stains—silver, methylene blue, gold—after birth; occurrence of dendritic pigmented cells simulating nerve cells in fetuses and after birth,[7] persistence of the same type of cell in tissue culture, with no resemblance or reversion to epithelial cells; resistance to roentgen or radium therapy of pigmented nevi and melanomas. This array of evidence gives great support to the theory of neural origin accepted by most workers today.

The most elementary benign lesion is lentigo, macular, and without nevus-cells, appearing on any part of the body, usually less than a centimeter in diameter, although it may be larger. It occurs with greater frequency relatively late in life, as discussed under "senile lentigo" by Cawley and Curtis.[8] However, brown macules seen shortly after birth or appearing in childhood are called "lentigo," and, when present in large numbers in a unilateral or bilateral distribution, are designated "lentigo profusa." Microscopically, lentigo shows only hyperpigmentation of the basal melanocytes and epidermis (Figure 1), without melanocytic proliferation. It is differentiated from nevus by the presence of large numbers of melanocytes in the latter.

Freckles (ephelides) are more common and lighter in color than lentigines. They appear in childhood after exposure to ultraviolet irradiation, and may or may not fade out in the winter. They are seen almost exclusively in light-complexioned or auburn-haired persons. The areas between the freckles may or may not pigment after exposure to ultraviolet irradiation. Biopsy reveals hyperpigmentation of the basal layer and epidermis, with slight or no pigment between the lesions. The melanin seems to be lighter in color than that in lentigo.

Among the most common pigmented lesions are pigmented nevi, formed by benign neoplasia of melanocytes at the epidermodermal junction. They usually appear during the first year or so of life as dark brown macules varying from a few millimeters to several centimeters in diameter. The dark brown color results from hyperpigmented nests (theques) of nevus cells at the epidermodermal junction (Figure 2), with accompanying melanosis of the epidermis. As the child grows, most nevi become elevated and less pigmented, because the theques change to lightly pigmented or nonpigmented nevus cells which penetrate into the dermis (Figure 3).

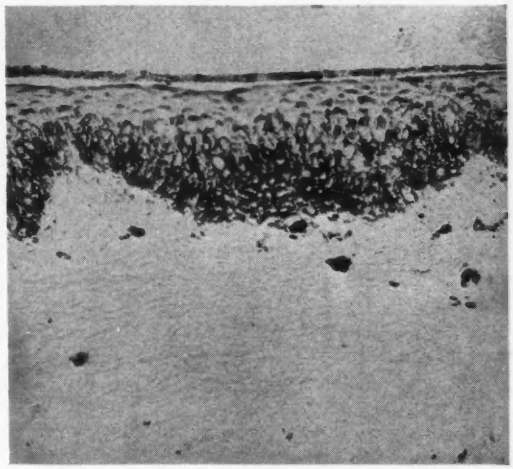

Figure 1.—Specimen of lentigo on cheek of 72-year-old woman. Melanocytic activity has produced simple hyperpigmentation. (Silver nitrate reaction.) (×200)

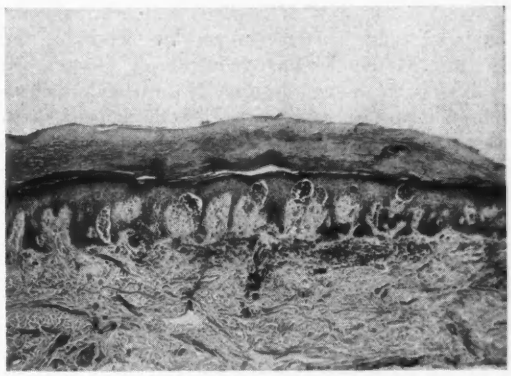

Figure 2.—Persistent theques in smooth nevus on sole of 32-year-old woman. The nevus cell nests are continuous with the epidermal cells. (Hematoxylin and eosin stain.) (×30)

The elevated, nonpigmented nevi are most frequent on the scalp, face and trunk, rare on the hands and feet. During childhood, some nevi darken and become blackish. Pronounced hyperpigmentation may be seen in biopsy specimens, which identifies the lesion as an "active" nevus, a term signifying hyperpigmentation, but not a tendency to malignancy. Biopsy should be done in the case of any nevus that is becoming appreciably darker, since inception of melanoma also causes darkening. In 80 to 90 per cent of cases, the status of a nevus is properly diagnosed by dermatologists.[3] There are many histologic variables in nevi. In infants, as studied by Stegmeier and Montgomery,[26] melanocytes are seen to have multiplied as oval or fusiform, hyperpigmented cells, and to form groups (theques) that are

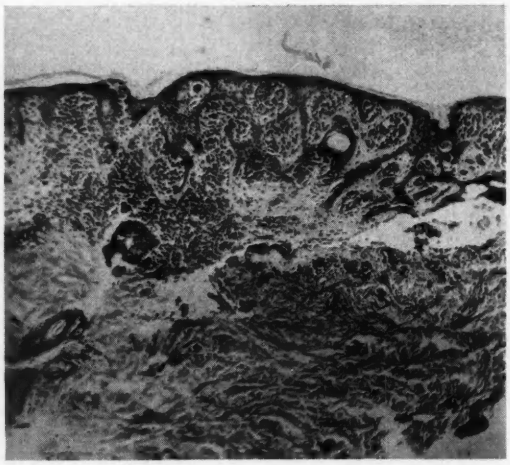

Figure 3.—Theques and dermal nests of nevus cells in 4-year-old child. (Hematoxylin and eosin stain.) (×35)

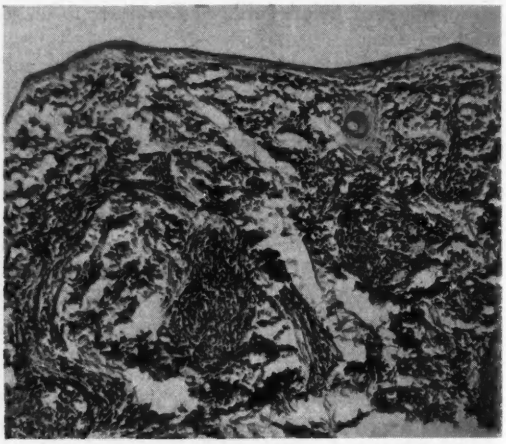

Figure 4.—Blue nevus. The fusiform melanocytes are separated from the epidermis by a thin layer of connective tissue. (Hematoxylin and eosin stain.) (×80)

at first intimately attached to the epidermis. Later, groups and strands of rounded and oval, smooth-surfaced cells penetrate to varying depths of the dermis. As they become more deeply located, the cells elongate, assume features of a variety of neurofibroma, and, in some cases, become lamellated to form "lames foliacees," which resemble Wagner-Meissner corpuscles. The only nevus cells that are pigmented are those nearest the epidermis, unless the tumor is a combined nevus and blue nevus, in which case some of the deeper cells are also melanotic.

Several attempts have been made to classify nevi on the basis of the microscopic appearance. The first was that of Traub and Keil,[27] as follows:

1. Junction-type nevus, with groups of nevus cells attached to the epidermis. Traub and Keil's illustrations (Figures 15 and 17 of their communication) strongly suggest lentigo maligna, which is in accord with their statement: "The growths that we have designated as junction type nevi represent what we consider potentially malignant melanomas."

2. Intradermal nevus, in which nevus cells are confined to the dermis.

3. Combination-type nevus, in which there is association of junction type with intradermal nevus.

The second classification was that of Miescher and Albertini.[17] The author modified the latter slightly as follows:[3]

(A) Lesions in which nevus cells are still definitely attached to, or actually integrated into the epidermis.

(B) Lesions in which no nevus cells are definitely attached to the epidermis, but are present in the dermis.

(C) Nerve nevus type of Masson, some portions of which resemble neurofibroma.

Of 741 nevi observed by me, there were 16 of the epidermal type (A); 65 with epidermal attachment in some areas, only dermal in others; 122 dermal only; 477 combining dermal and neural areas; 49 with features of all three types, and 12 that were purely neural.

Lund and Stobbe[14] made additional subdivisions into five groups instead of three. None of the above classifications includes blue nevi or combination of nevus and blue nevus. This combination is of importance because it has been mistaken for melanoma.

Blue nevus, an acquired bluish macule or maculopapule, usually a few millimeters in diameter, rarely larger, and sometimes gradually increasing in size (progressive blue nevus), is blue in color because the brown, melanin-containing fusiform cells are located so deep in the dermis that the scattering effect of the overlying tissue produces a blue hue. A blue nevus of special distribution is known as fuscoceruleus ophthalmomaxillaris, or nevus of Ota, since it was studied by him and later by Ito.[13] The dermal melanocytes producing the blue nevus originate from the deeper of the two pigment-cell layers. If they are more superficial and hug the epithelium (Figures 4 and 5) the color may be brownish or blackish. If inflammation has developed, the color may be very dark, because of melanin in melanophages.

Bluish "sacral spots" are also known as "mongolian spots" because they are seen in the sacral and adjacent regions (at times more caudad on the dorsal surface, rarely on the ventral surface of the body) of practically all newborn babies of the mongolian races, and to a somewhat lesser degree in

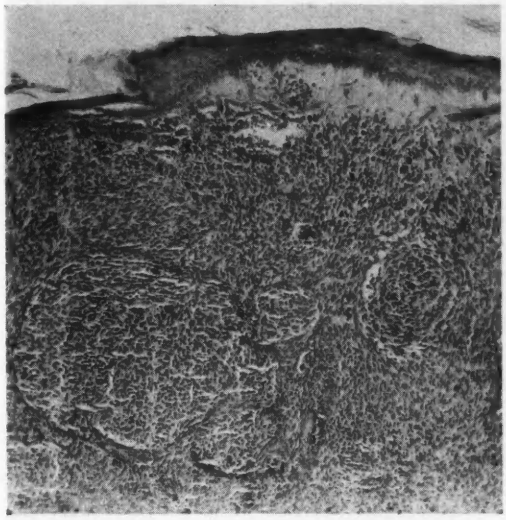

Figure 5.—Blue nevus, part of which is lightly pigmented. (Hematoxylin and eosin stain.) (×75)

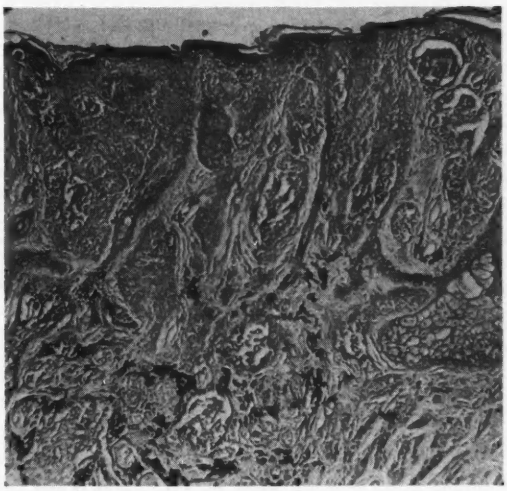

Figure 6.—Combined nevus and blue nevus in 18-year-old patient. (Silver nitrate, pyronin-ethyl green stain.) (×40)

other dark races. They are formed by the same fusiform melanocytes as are blue nevi, but differ in that their cells are less concentrated and in their tendency to disappear slowly during early childhood.

Combined nevus and blue nevus, infrequently found on biopsy of elevated pigmented nevi (a little less than 1 per cent in the author's series), may be blackish in all or part of the lesion. The superficial nevus cells are of the usual variety, arising from the superficial melanocytic layer, while the blue nevus cells, usually fusiform, arise from the deeper layer, hence are seen in the deeper portion of the nevus (Figure 6). This combination seems to account for the occasional finding of pigmented melanocytes in the deeper portion of nevi, among the nonpigmented dermal nevus cells.

Probably belonging to nevi, although not manifest at birth, "juvenile melanoma" (Spitz) has characteristics of both benign nevi and malignant melanoma. Pack,[21] who was first to describe such growths, stated that they are deeply pigmented, but Spitz[25] reported mildness of pigmentation, which conforms to the experience of the present author and of others. Microscopically these tumors resemble nevi for the most part, and probably never become malignant. The present author has observed that the characteristic cells are mildly dopa-positive, which seems to confirm a melanocytic origin, and therefore prefers to call the tumor "pseudomelanoma."

The most important brown or black neoplasm is a malignant melanocytic tumor for which at least 16 names have been suggested. Unna believed this growth was of epithelial origin, and so did Bloch, Darier, Allen[1] and other investigators. Unna termed it a "nevocarcinoma," implying that it arises in a benign nevus which has, in turn, originated from epithelial cells—hence the classification as carcinoma. However, since the melanocyte is now believed by most workers to be of nonepithelial origin, a malignant tumor arising from it should be called a sarcoma; therefore Kaposi was correct in 1895 when he applied the term "melanosarcoma." For this presentation, though, the most common designation, "melanoma," will be used. This was suggested by Carswell in 1838, some British[12] and Australian investigators prefix "benign" in the case of a pigmented nevus, distinguishing it from the malignant melanoma.

Melanoma arises in at least three ways: (1) In pigmented nevi, (2) from normal skin, and (3) as lentigo maligna. Opinions on the proportionate frequency of each source vary widely: Pack[22] thought that all melanomas come from nevi, and Allen[1] traced them "almost exclusively from junctional nevi or from junctional component of compound nevi," while others attributed smaller proportions to this source—as few as 18 per cent, according to Daland and Holmes.[9] At the University of Chicago's dermatological pathology laboratory, the author found evidence of neval origin in only 23 per cent of specimens. Melanoma sometimes arises in what appears to be normal skin, and could be called "melanome d'emblee." Pillsbury, Shelley and Kligman[23] emphasized, "It is not sufficiently appreciated that melanocarcinoma arises without any preceding lesion in some 25 per cent or more cases." This estimate seems to be somewhat high.

Most melanomas arise in the form of a brownish plaque, known as "lentigo maligna," which starts

as an asymptomatic brown macule, usually but not always late in life, enlarges slowly over months or years, and shows varying shades of brown in the same lesion, with some areas blackish. Eventually, at some point in the plaque, a tumor arises—either erythematous, resembling granuloma pyogenicum, or blackish. Appearance of the tumor presages the presence of metastasis, as studied by deMorgan and reported by Handley.[11]

Use of the terms "junction type mole" or "junction nevus" has been discussed by the author,[4] who believes they should be abandoned. The chief reason is that these designations have been applied to two benign lesions, quiescent nevus and active nevus, and to one malignant lesion, lentigo maligna. The first two show only benign neoplasia; the last-named is distinguished from nevus by the malignant neoplasia of the melanocytes, which first work their way to the cutaneous surface. There is abundant lymphocytic infiltrate, which is never found in a nevus except in a case of injury or infection. Many observers have assumed that melanomatous tumor arises in the so-called "junction" nevus, evidently from the nevus cells. The author has never seen evidence for such an origin, and questions whether benignly neoplastic nevus cells ever become malignant. Melanoma arises in a nevus in about 25 per cent of cases, but in the specimens studied the origin seemed to be in the form of malignant neoplasia of melanocytes at the epidermodermal junction and not from preexisting nevus cells. The clinical signs of malignant melanocytic degeneration in a nevus are enlargement and darkening of the lesion. The tumor becomes more fragile, oozes, and later bleeds easily.

Confusion has resulted from including all pigmented precursors of melanoma, both pigmented nevi and lentigo maligna, under the designation "moles," which thus includes 75 per cent or more. That the epidermodermal junction of a pigmented nevus is a prominent origin for melanoma may be determined by contrasting the surface of the body, about 2,000 sq. cm., with the surface of the ten to twenty pigmented nevi on the average adult. Even if a minimum of 25 per cent of melanomas arise in nevi, this small surface assumes relatively great importance in the origin of melanoma.

The clinical appearance of melanoma varies from a coal-black tumor to an erythematous granuloma-like tumor, depending on the degree of pigmentation. The nonpigmented tumors become black when placed in a solution of tyrosine, as shown by Fitzpatrick.[10] Clinical diagnosis is made in less than 50 per cent of cases—in 48 per cent of one series diagnosed microscopically, in the author's experience,[5] and in 38 per cent of McMullan and Hubener's series.[18] It is therefore obvious that biopsy

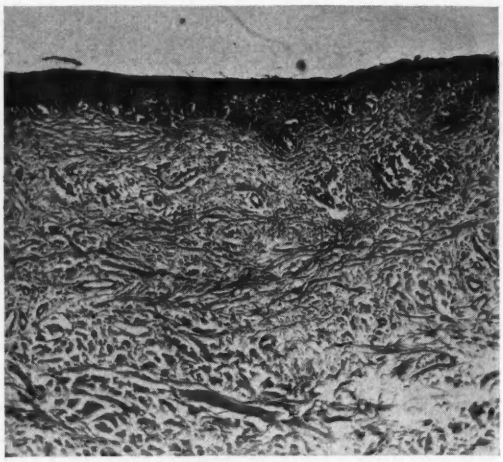

Figure 7.—Lentigo maligna. Section from brown border of lesion of unknown duration on scapular region of 82-year-old man. Melanocytes have undergone malignant neoplasia. Lymphocytic infiltrate is present. (Hematoxylin and eosin stain.) (×60)

is of utmost importance. Regarding the safety of biopsy of melanoma, Osborne[20] stated, "I have never seen a case in which biopsy could be incriminated as the cause of metastasis." The author agrees with this concept and has always biopsied melanoma. Several investigators, including surgeons, recommend removal of the entire lesion, to which there can be no valid objection.

Upon microscopic examination of melanoma, whether arising in lentigo maligna, in normal skin or in a pigmented nevus, one may see malignant melanotic cells, first at the epidermodermal junction (Figure 7) whence they are often carried in groups in the epidermis to the surface. Later, they penetrate into the dermis (Figure 8). Abundant lymphocytic infiltrate is present in the superficial dermis. The malignant cells are round, oval or fusiform, and usually contain some melanin, often very much, in form of granules the size of which is uniform in any individual cell. In the tumor stage, malignant cells of melanocytic origin may be seen growing outward against an epidermis thinned by pressure of the tumor. Mitotic figures, rare in the pretumorous stage, may be numerous in the tumor stage and associated with pronounced cellular anaplasia. Nonpigmented melanoma may contain no melanin, but may be slightly pigmented with hemosiderin. However, if studied by the silver nitrate method of Bizzozerro[6] melanin granules may be found, often only in melanophages. Metastatic tumors usually contain more anaplastic cells than the primary cutaneous tumor.

Metastatic pigmented melanoma is likely to occur in any tissue of the body, including the skin, either

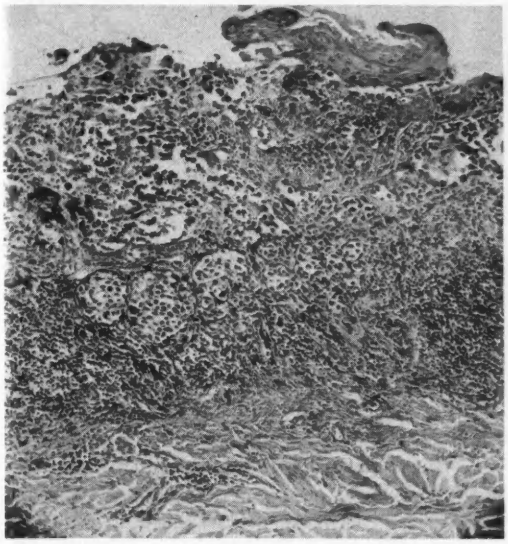

Figure 8.—From black elevated area of lentigo maligna, same lesion as in Figure 7. Melanoma cells are penetrating into the dermis. Pronounced lymphocytic infiltrate. (Hematoxylin and eosin stain.) (×75)

in the form of local satellite tumors as reported by Madden[15] between the primary site and regional lymph nodes, or as widely disseminated black or lighter tumors over any part of the body. Histologically they are not unlike a primary melanoma with so-called "junctional activity," as reported by Nicolau and Darier[19] and others, but denied by Allen.[1]

Microscopic differentiation must be made from lentigo, pigmented nevus, blue nevus, melanotic seborrheic keratosis, melanotic carcinoma, hemosiderotic histiocytoma, thrombosed hemangioma and other blood-containing tumors. Nonpigmented melanoma must be differentiated from pyogenic granuloma, juvenile melanoma (Spitz) and other nonpigmented tumors.

COMMENT

From the practical viewpoint, disregarding differences of opinion relative to the origin of nevus cells and melanoma cells, microscopic examination must supplement clinical diagnosis of melanoma and related tumors. At present, it is only in this way that accurate diagnosis may eventually be attained. Consultation is advisable on any microscopic section that suggests the diagnosis of melanoma. The life history of the neoplasm, with its many vagaries, should be appreciated by the pathologist, so that the best possible therapeutic management for any stage of the disease may be recommended. In this way, the prognosis can be improved.

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Hip Pinning

A New, Rapid and Accurate Method

GEORGE E. REY, *M.D.*, Porterville

USE OF FIXATION with nails or pins to hold bone fragments together is one of the great improvements that has been developed in the past 20 years for dealing with fractures of the hip. There are many kinds of fixation apparatus, almost all with merit, but there has not been much improvement in methods of introduction of the pins or nails. Making drill-holes in the right direction and proper introduction of the pins is often difficult and necessitates multiple radiographs during the procedure. Sometimes these difficulties greatly extend the time the patient has to be kept in anesthesia.

In 1946 I devised an instrument (Figure 1) for directing the guide-pin, and I have used it since then in all patients who have been in my care and often in placing guide-pins for other physicians. In no case was the pin ever out of line in any direction. When this instrument is used, the only x-ray film taken during the operation is to make sure the pin is the right length. If careful measurements are taken and the necessary length can be definitely ascertained before operation roentgenograms during the procedure may be dispensed with. It was never necessary in any of the cases to change the position of the guide-pin once it was placed. Figure 2 is an x-ray film taken in a case in which the instrument was used.

Submitted March 8, 1957.

Figure 1.—Photograph of device for placing guide-pins in the femur in procedures for fixation of fractures of the hip. Size of device can be judged from inset showing it held in surgeon's hand.

METHOD

After accurate reduction of the fracture, the blades of the guiding device are separated and applied about the neck of the femur, one at a time, through a small incision in the anterior surface of the capsule. The blades are then locked, the pin inserted through the guide holes, as shown, and drilled to the depth previously determined. With this method, the guide pin must always hit the center of the neck of the femur, regardless of the size of the bone. At this point an x-ray film is made for exact determination of depth of penetration. The nail is then driven over the guide-pin in the usual manner.

603 North Hockett Street, Porterville.

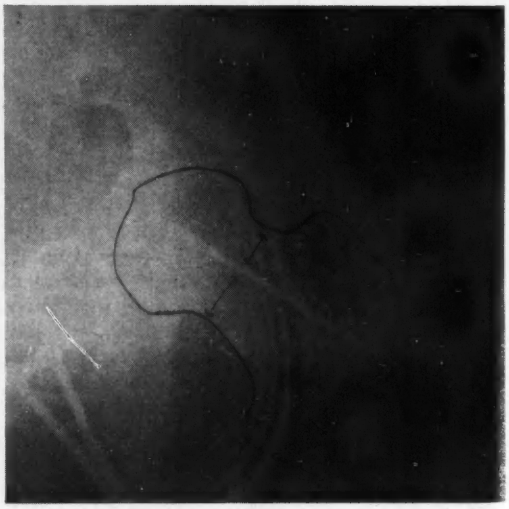

Figure 2.—Placement of pin in an intertrochanteric fracture in a 73-year-old woman. This was the only x-ray film made during operation.

Post-traumatic Superior Laryngeal Neuralgia

WILLIAM F. BAXTER, M.D., Sunnyvale

• **Several years after tonsillectomy—or more quickly after foreign-body trauma—the superior laryngeal nerve may be so bound by fibrosis that any regional inflammation or further local trauma, aggravated by normal laryngeal movements, can give rise to localized neuritis at the thyrohyoid membrane and cause a characteristic pain.**

In every one of 21 patients observed in the past five years, a point of tenderness was readily found by digital palpation over the lateral portion of the thyrohyoid membrane or over the superior cornu of the thyroid cartilage. Frequently the pain extended into the throat and became worse as anything was swallowed past this point.

Medical therapy alone or with external injection followed by five minutes of local massage relieved the pain in most cases. It seems possible that, in a more recalcitrant case, relief could be obtained by incising the thyrohyoid membrane so as to relax the superior laryngeal nerve.

MOST PHYSICIANS have treated patients for throat soreness with localized tenderness at one of the lateral edges of the thyrohyoid membrane. The author, after observing 21 instances of such regional pain during the past five years, concluded that these symptoms were due to superior laryngeal neuralgia. Since most patients recover after nonspecific therapy, the entity has not been closely scrutinized, nor its cause identified; but for the sake of those few patients with serious and refractory pain, a more definitive treatment is worth considering.

Little has been written about superior laryngeal neuralgia in recent years. Not long ago it was most often encountered in tuberculosis of the larynx and was treated with local ultraviolet rays or with alcohol injection of the nerve.

Cortesi[3] studied the effect of laryngeal nerve stimulation on vital functions in animals, and he noted that a strong stimulus caused a decrease in respiratory function, whereas a weak stimulus caused an increase. Electrical stimuli caused slight arterial hypertension, while chemical or thermal stimuli caused hypotension and bradycardia. The results were the same whether the stimulus was applied to the superior laryngeal nerve or to the laryngeal mucous membrane.

When De Kleyn[4] injected alcohol into the superior laryngeal nerve of a 34-year-old patient, earache on the injected side followed almost immediately, and the blood vessels in the eardrum became engorged. De Kleyn felt that there were aberrant nervous impulses along the nervus auricularis vagi.

Ogura and Lam[7] applied electrical stimulation to the superior laryngeal nerve in volunteer unanesthetized patients just before operations involving laryngectomy, and later compared their findings with microscopic studies of the excised nerves. They estimated that the superior laryngeal nerve contains about 15,000 myelinated fibers and 1,000 unmyelinated. The largest fibers (10 to 15 micra) made up one-third of this count but occupied about five-sixths of the total cross section of the nerve. The remaining one-sixth of the cross section was taken up by many small fibers (1 to 3 micra), numbering about half the total count, and fewer fibers of intermediate size numbering the remaining sixth. Milder stimulation, these investigators found, affected the large and medium-sized myelinated fibers carrying impulses at about 50 meters per second; sensations of pain and touch were produced. Stronger stimuli activated the thinly myelinated fibers at about 15 meters per second, causing pain. Very strong repetitive stimulation activated the smallest myelinated and the unmyelinated fibers carrying impulses at about 1 meter per second, giving rise to boring and deep burning pain, mucous secretion, swallowing movements, sudden closure of the vocal cords and apnea. This strong reaction, the investigators believed, was motivated through both direct and reflex pathways. None of the patients noted any taste sensations, but the investigators conjectured that taste if present might have been masked by the pain.

Bertoin[2] in 1946, discussing what he called "essential" neuralgia of the superior laryngeal nerve, presented a view quite similar to my own. He too felt the condition was not usually recognized as such, and believed it may follow laryngitis, angina, or, most commonly, influenza. Besides pain, he mentioned coughing and vocal instability as symptoms. He describes as pathognomonic a painful spot where the superior laryngeal nerve passes through the thyrohyoid membrane. He treated the condition satisfactorily by heat, by anesthetizing the piriform

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TABLE 1.—*Clinical Data and Notes on Pathogenic Factors and Treatment in 21 Cases of Post-traumatic Superior Laryngeal Neuralgia*

Case	Sex	Age	Side	Previous Operation	Radiation	Cough	Length of Present Illness	Pertinent Past History	Examination	Treatment	Outcome
1.	M	55	Rt.	T.	Rt. ear	No	1 week	.....	Not remarkable.	B-complex tablets, B_{12} injections intramuscularly.	Well in 1 week.
2.	F	47	Rt.	T.	.....	No	1 week	Ulcer history, frequent headaches. Vocal instability.	Tonsil stub on rt., slight amount of pale edema of the vocal cords.	Xylocaine® injections and massage. Stomach and nerve relaxants.	Larynx appeared normal after 8 days. Pain a few hr., then well 3 mo. later.
3.	M	45	Lt.	T.&A. twice	Lt. ear	No	4 years	No help from "antibiotics," thyroid or throat spray.	Right tonsil stub red. Enlarged lingual tonsil.	Topical anesthesia no help. Xylocaine and massage 5 times in 2 months.	Gradual improvement. Well 7 months later.
4.	F	56	Rt.	T.	Rt. ear	Slight	1 week	.....	Slightly red posterior wall of hypopharynx.	B-complex tablets and cough syrup.	Gradually well in 1 week.
5.	M	45	Lt.	T.&A.	Lt. ear	No	3 weeks	Upper respiratory infections start as laryngitis. 3 mos. trumpet practice aggravated condition.	Not remarkable.	Avoid strain.	No follow-up.
6.	F	71	Rt.	T.&A.	Rt. ear	No	1 week	.....	Impacted cerumen, rt.	External heat and throat irrigation.	Palsy of rt. hypoglossal nerve developed. Neck well in 2 months.
7.	M	72	Rt.	None	Rt. side of face	No	6 months	Heart disease.	Nodule lower pole rt. thyroid.	Pain better with topical anesthesia in hypopharynx.	Well in 3 weeks.
8.	M	42	Rt.	T.	Rt. ear	No	4 days	2 attacks, 1 with upper respiratory infection, 2 upon overactivity.	Diffuse pharyngitis.	Antibiotics and rest.	Well in 1 week each time.
9.	M	35	Rt.	T.&A.	None	Mod.	10 days	Traveling salesman, heavy smoker.	Tonsil stubs, enlarged lingual tonsil, red hypopharynx and vocal cords.	Stopped smoking.	No follow-up.
10.	F	50	Rt.	T.	None	No	6 months	Has had potassium iodide, "antibiotics" and dental extractions.	Red lateral bands, epiglottis, and edema of rt. arytenoid.	Topical anesthesia in hypopharnx helped.	Gradually cleared.
11.	F	45	Lt.	T.	Lt. ear	Severe 1 month	1 year	Pain with upper respiratory infection in cold weather. Moderate smoker.	Not remarkable.	B_{12} injections, multivitamins, cough syrup.	Better in 10 days.
12.	M	55	Rt.	T.	Rt. ear	Mod. 3 weeks	6 weeks	20 yr. before, pain in throat and rt. ear 2 mo. after operation. Cicatrix treated by massage.	Small cyst anterior surface left side epiglottis.	Xylocaine injection and massage.	More pain for 2 days. Then better by 2 weeks.
13.	F	46	Rt.	T. twice	Rt. ear	No	2 months	Rt. otitis media acute purulent, age 20. Fell on rt. neck and arm with pain into rt. ear age 42. Rt. Meniere's at age 43.	Not remarkable, except for dark thick rt. ear drum.	Antibiotics and rest.	Gradually cleared in several weeks.
14.	F	43	Lt.	None	Lt. ear	Slight	2 years	See case report (Case 1).	Not remarkable.	Xylocaine inject., massage. B_{12} intramuscular, multivitamins.	Foreign-body fixation. Psychosis developed.
15.	M	53	Rt.	T.	Rt. ear	Slight	5 years	Pain with all upper respiratory infections. Recent bronchoscopy. Heavy smoker.	Tonsil stubs bilateral. Enlarged lingual tonsil. Cyst, rt. anterior surface of epiglottis.	Antibiotics and rest.	Well in 1 week.
16.	F	74	Lt.	T.; sinus	Lt. ear	No	2 years	Sinus operation age 57.	Not remarkable.	Xylocaine injection and massage.	Better since injection.
17.	F	50	Rt.	None	.....	No	3 years	3 years before, choked on a chicken bone. Pain with all upper respiratory infections since. Vocal instability.	Red rt. vocal cord. Normal movement.	Xylocaine injection and massage. Penicillin nebulizer.	Gradually improved.
18.	M	39	Lt.	T.	Lt. ear	No	2 weeks	Heavy smoker.	Not remarkable.	Stopped smoking.	Well next visit 4 mos. later.
19.	M	53	Lt.	None	None	No	2 years	Moderate smoker. Heavy smoker 2 years ago.	Chronic purulent tonsillitis.	Tonsillectomy no help. Xylocaine injections and massage.	Gradually improved.
20.	F	64	Rt.	T.	None	Slight	5 years	Repeated pharyngitis.	Slight lateral-band pharyngitis.	Topical anesthesia helped. Massage, heat. B_{12} injections.	Well 1 month later.
21.	M	39	Lt.	None	Lt. side neck	No	1 year	Several years of pain with tonsillitis.	Mild tonsillitis.	Penicillin, Xylocaine and intramuscular B_{12} injections.	Well in 1 week.

sinus, or by external injection at the point of maximum tenderness.

As shown in Table 1, summarizing the cases of 21 patients with superior laryngeal neuralgia, the majority were in the fourth or fifth decade of life, the youngest aged 35 years. The sexes were equally represented. Significant perhaps is the fact that all the patients were right-handed, and that in 13 of the 21 the pain was right-sided.

Sixteen patients (76 per cent) had had previous throat operations—in every case many years before onset of the neuralgia. Two others dated the tenderness in the neck from a time when they had choked on a chicken bone. Thus, altogether 86 per cent had had surgical or other trauma to the throat. Only three patients were heavy smokers, and a reduction in smoking eased the pain. Cough was not mentioned by most patients, but six had had a cough for a variable time just before the onset of neuralgia, and apparently precipitating or contributing to it. An unusual precipitating cause was trumpet playing, which the patient had resumed, after many years' lapse, three months before onset of pain; the pain was so severe during playing that when last seen the patient felt he would have to give it up.

In every patient, a point of tenderness was readily found by digital palpation over the lateral portion of the thyrohyoid membrane or over the superior cornu of the thyroid cartilage. Frequently the pain extended into the throat and became worse as anything was swallowed past this point. Three patients had only this localized pain; in 13 the pain radiated to the ipsilateral ear, and in one it extended over the same side of the face. Two patients reported a variable or breaking voice, but they did not mention hoarseness. This vocal change might indicate some dysfunction of the cricothyroid muscle innervated by the external branch of the superior laryngeal nerve rather than the kind of dysfunction resulting in laryngitis.

When first seen, the patients had had neuralgia for periods of a week to five years. In cases in which the pain had been occurring for six months or more, it was usually associated with respiratory infections. On otolaryngologic examination eight patients appeared relatively normal; eight had some pharyngeal or hypopharyngeal inflammation involving, in a few, tonsil stubs or enlarged lingual tonsils. In four patients, laryngeal areas were inflamed; two appeared to have benign cysts on the anterior surface of the epiglottis, and one had a nodule in the lower pole of the thyroid on the painful side.

Treatment of these patients is detailed in Table 1. The neuralgia, it is felt, may be self-limiting in many cases, although in general the longer the pain has been present, the more difficult it is to relieve completely.

Two cases seem worth reporting more fully:

CASE 1 (No. 14 in Table 1): A 43-year-old house servant had choked on a chicken bone two years before she was first seen, and had a fixed idea that some of the bone was still in her throat. Shortly after the choking episode she had been told, before undergoing tonsillectomy, that the chicken bone would be removed at operation. Since the localized pain in the area of the left thyrohyoid membrane persisted after tonsillectomy, roentgen studies were made but did not show any foreign bodies, nor did laryngoscopy and esophagoscopy under general anesthesia, done by a thoracic surgeon. At this time the patient felt that the bone was gone but that a piece of glass was stuck in the same site. The pain could be temporarily relieved by anesthetic injection about the superior laryngeal nerve, but the patient persisted in her fixed idea that a foreign body was lodged in her throat. Other mental aberrations became evident, and psychiatric consultation was advised.

CASE 2 (No. 19 in Table 1): A 53-year-old man had for two years had recurring pain in the left side of the throat, worse at night and in the early morning, with no radiation to other areas. Up to ten months before he was first seen, he had been smoking about two packs of cigarettes a day, but recently he had been smoking only a couple of cigars a day. On initial examination the throat appeared normal except for the tonsils, which were small but yielded liquid pus from the crypts on pressure, and an area of point tenderness over the left thyrohyoid membrane. A diagnosis of chronic tonsillitis and superior laryngeal neuralgia was made. Tonsillectomy was done by a hospital resident, and there was considerable postoperative pain radiating into the left ear. Three months later the patient was treated for pain in the left trapezius muscle from cervical arthritis. Six months after tonsillectomy he returned complaining of the same pain in the left thyrohyoid membrane area, gradually increasing for the preceding three months. This was relieved by injection of the left superior laryngeal nerve, and subsequent injections for recurrence were given after intervals of ten days, six weeks and three weeks. The pain lessened after each injection, and a year after the fourth injection the patient had not returned.

DISCUSSION

In understanding the problem of pain arising from the superior laryngeal nerve, it is important to keep in mind the anatomical course of the internal branch of this nerve from the mucous membrane of the supraglottic, epiglottic, base of the tongue, and medial parts of the piriform sinuses through the thyrohyoid membrane to the noduse ganglion of the vagus nerve (Figure 1). Between these two latter structures, the nerve branch passes posteriorly, superiorly, and a little laterally, outside the middle

21.	M	39	Lt.	None	Lt. side neck	No	1 year	Several years of pain with tonsillitis.	Mild tonsillitis.	Procaine, Xylocaine and intramuscular B_{12} injections.	Well in 1 week.

pharyngeal constrictor muscle and the stylopharyngeus muscle to the vagus nerve (Figure 2). The glossopharyngeal nerve is superior to the superior laryngeal nerve and has many branches going to the pharyngeal musculature and to the base of the tongue for taste discernment. The glossopharyngeal nerve passes very close to the lower pole of the tonsil and is separated from it only by the thin fibers of the palatopharyngeus muscle in one area.

The superior laryngeal nerve, lying more inferior and outside more muscle tissue than the glossopharyngeal nerve, can still be involved in a roughly done tonsillectomy. If the muscular bed of the palatine tonsil is torn, especially at the lower pole, there will certainly be more fibrosis and retraction. The glossopharyngeal nerve and the superior laryngeal nerve may both be caught in some of the fibrosis resulting after tonsillectomy. Whereas the function of the glossopharyngeal nerve is not impaired if fibrous tissue pulls it one way or another, the internal branch of the superior laryngeal nerve may well be affected by fibrous retraction, for the retraction may shorten and kink the nerve where it penetrates the fibrous, unyielding thyrohyoid membrane. Several years after tonsillectomy—or more quickly after foreign-body trauma—the superior laryngeal nerve may be so bound that any regional inflammation or further local trauma, aggravated by normal laryngeal movements, can give rise to localized neuritis at the thyrohyoid membrane and cause the pain previously described. One way to test this theory would be to incise the thyrohyoid membrane so as to relax the superior laryngeal nerve, rather than to resect a portion of the nerve as has been done at the Mayo Clinic.[9] Until such an approach can be validated in suitable cases, medical therapy alone or with external injection followed immediately by five minutes of local massage relieves the pain in almost all patients.

Several other conditions which must be considered with pain in the neck or throat before making a diagnosis of superior laryngeal neuralgia are glossopharyngeal neuralgia, laryngeal perichondritis, neoplasms, cervical arthritis, fibromyositis, globus hystericus, and pain from the autonomic nerves associated with the local blood supply.

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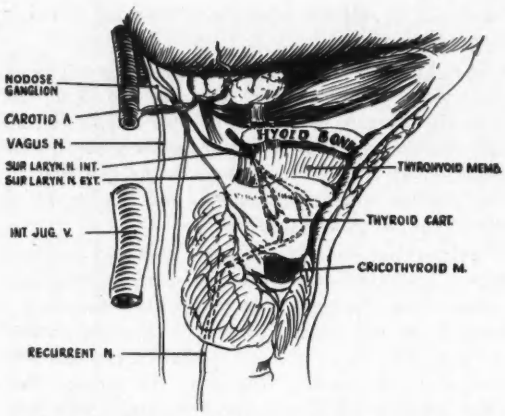

Figure 1.—Passage of the superior laryngeal nerve through the thyrohyoid membrane.

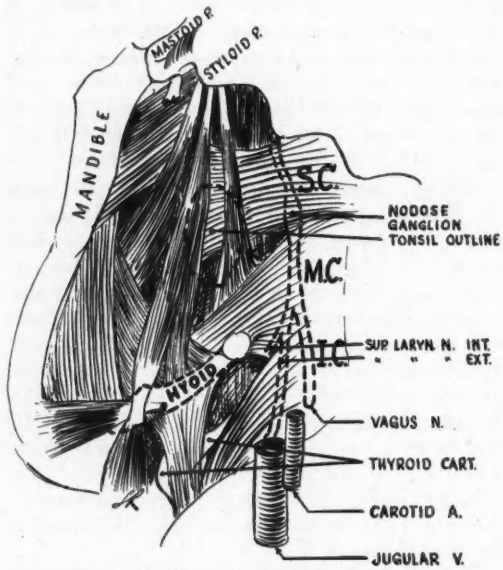

Figure 2.—Posterolateral view showing relation of vagus nerve and branches to pharyngeal musculature. S.C. = Superior constrictor; MC = Middle constrictor; I.C. = Inferior constrictor.

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Discussion by **MARIO ACQUARELLI, M.D., Los Angeles**

Dr. Baxter has brought to light a clinical diagnosis of a condition which some of us have seen; we can recall the symptoms and findings but perhaps the condition did not stimulate us to the point of further study or investigation.

In Denker and Kahler's "Handbook of Ear, Nose and Throat"[1] Boeninghaus (1) described a case and called it "nervous pain of the throat." He based his diagnosis on typical localized painful pressure points in the lateral part of the thyrohyoid membrane, and (2) on the lateral side of the trachea, the latter location being the recurrent laryngeal nerve pressure point. In the same textbook, Amersbach stated that true neuralgias of the superior laryngeal nerve cause severe subjective complaints and that the origin may be central or peripheral (neuritis). He had in some cases isolated typical pressure points which did not correspond with localization of pain as described by the patient. Amersbach cited Gottstein's report of one patient who experienced superior laryngeal neuralgia only while talking. Another contributor, Schnitzler, described a case with anesthesia and pain and called it "anesthesia dolorosa." The pain as described by Schnitzler was burning and lancinating in character with radiation to the ear.

Therapy, as summarized by Amersbach, consisted of the generally prescribed antineuritics. For refractory cases, injections of ½ to 2 per cent novocaine solution into the superior laryngeal nerve were recommended, and for the most severe cases, alcohol injection or severance of the superior laryngeal nerve was reported successful in the absence of a central lesion.

I have observed superior laryngeal neuralgia in patients with tuberculosis or carcinoma of the larynx. Therapy consisted of injections or section of the superior laryngeal nerve. In the future I will be on the alert for this condition, thanks to Doctor Baxter's timely paper on this subject.

596 South Carroll Avenue, Sunnyvale.

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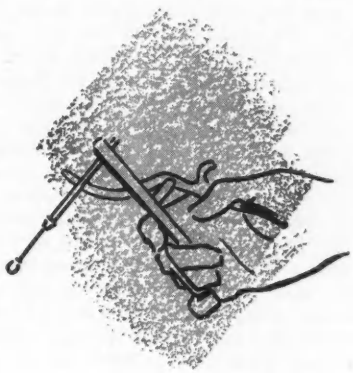

Adenocarcinoma of the Lung Treated with X-Ray and Nitrogen Mustard—Five Years From Discovery to Death

JOSEPH J. ARONS, *M.D.*, San Rafael
ALBERT C. DANIELS, *M.D.*, San Francisco, and
RUSSELL W. BERNHARD, *M.D.*, San Rafael

IT IS THE PURPOSE of the following case report to suggest that in dealing with carcinoma of the lung, x-ray therapy, in conjunction with surgical excision or chemotherapy or by itself, can improve the present therapeutic results. Moore[3] reported survivals of seven years in one case and nine years in another with x-ray therapy alone. At the time this report was written, Roswit[5] was observing one patient with mucoepidermoid carcinoma of the lung that was considered inoperable at the time of diagnosis. X-ray therapy, 3,500 r, was given and the patient has survived nine years to date. Burnett[2] reported one patient surviving nine years with x-ray therapy. Smart and Hilton[6] reported that eight patients of 203 who (with a few exceptions) had inoperable pulmonary carcinoma, survived more than five years with x-ray therapy alone. One of the patients in the series had an operable lesion but refused operation and another had severe chronic bronchitis which made x-ray therapy seem more judicious. Brooks[1] reported the following survival times of 306 patients, all with histologically confirmed carcinoma of the lung, who were treated by various methods:

Treatment	1 to 2 Years	2 to 3 Years	Over 3 Years
X-ray	45	12	4
Surgical operation	9	5	2
Chemotherapy	5	0	0
X-ray and chemotherapy	6	2	0
Not treated	3	0	0
Operation and x-ray	3	0	0

In a personal communication dated August 6, 1957, Smithers[7] reported cases in which patients with carcinoma of the bronchus lived five years or more following radical x-ray therapy (Table 1).

In appraising the end results in treatment of cancer of the lung, Overholt[4] gave the data shown in Table 2 which include the five-year survival rates from time of treatment.

Recently there have been reports in the literature of five-year survival with the use of x-ray therapy alone. Perhaps, only patients with "inoperable" cancer should be treated by x-ray only, or x-ray and chemotherapy, but is this necessarily so? An additional case of prolonged survival with treatment by x-ray supplemented by nitrogen mustard therapy is herewith submitted. In retrospect, the patient presumably had a bronchogenic carcinoma for at least one year before therapy was instituted. X-radiation was begun four years and ten months before the death of the patient. At the time of bronchoscopy in October, 1949, it was decided that the lesion was inoperable. It was then, only as a means of palliation, that roentgen radiation therapy was given. When symptoms recurred almost three and a half years later, x-ray therapy was again given and this treatment was supplemented by nitrogen mustard therapy. The patient then lived for an additional period of a year and a half. For the last 20 months of his life, he had complete atelectasis of the right lung with compensatory shifting of the mediastinum. The heart shifted entirely to the right side of the chest. The results of x-ray therapy were so good that for several years there was a disturbing question as to whether the patient had ever really had a carcinoma. This case is presented in the hope that x-ray therapy will not necessarily be looked upon as a last resort. In view of the natural variation of bronchogenic carcinoma, many patients might well survive as long or longer with x-radiation as with surgical therapy. (The case here reported may be regarded as one at the favorable end of the spectrum of treatment.)

REPORT OF A CASE

The patient, a man 74 years of age, was first observed August 2, 1949. He complained of an intermittent cough of two to three years' duration which, although worse during the night, was present at all times. This caused severe insomnia and wheezing, without, however, any definitive cardiorespiratory symptoms. The past history was not significant except for notably long-lived ancestry, the patient's father having died at the age of 94 and his mother at the age of 86. He had three brothers, all in their seventies, all living and well, and one sister who had

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TABLE 1.—*Survival for More Than Five Years Following Radical X-ray Therapy for Patients with Carcinoma of the Bronchus (Smithers')*
(Follow-up from date of first treatment to end of December 1955)

Year	Number alive at the end of										
	5 Yrs.	6 Yrs.	7 Yrs.	8 Yrs.	9 Yrs.	10 Yrs.	11 Yrs.	12 Yrs.	13 Yrs.	14 Yrs.	15 Yrs.
1940	1	1	1	1	1	1	1	1	1	1*	
1941											
1942											
1943											
1944	1	1	1	1	1	1	1		Anaplastic carcinoma.		
1945											
1946	1	1	1	1		Unconfirmed histologically, but died of multiple metastasis.					
1947	2	2	2	2	One with squamous-cell carcinoma had pneumonectomy following irradiation. One unconfirmed histologically, was found to be inoperable at thoracotomy.						
1948	1	1	1		Squamous-cell carcinoma.						
1949	1	1			Oat-cell carcinoma.						
1950	1				Squamous-cell carcinoma.						

*Squamous-cell carcinoma; died of intercurrent disease with no sign of recurrence.

TABLE 2.—*Overholt's[1] Review of Treatment of Cancer of the Lung at Various Stages by Various Methods*

Treatment	When the Lesion Was Localized		When the Lesion Was Regional		When There Were Metastases		When Lesion's Extent Unspecified	
	Cases	5-Year Survival	Cases	5-Year Survival	Cases	5-Year Survival	Cases	5-Year Survival
Surgical	467	133—29%	584	59—10%	150	3— 2%	146	37—25%
X-ray	77	0— 0%	131	2— 2%	157	0— 0%	389	7— 2%
Surgical and x-ray	15	2—13%	50	7—14%	26	0— 0%	25	2— 8%
Other or none	356	6— 2%	575	1—0.2%	1562	2—0.1%	969	32— 3%
	915	141—15%	1340	69— 5%	1895	5—0.3%	1529	78—4.7%

died at the age of 68 of "heart trouble." For sixty years the patient smoked from one to two packages of cigarettes every day. He insisted that the cough was definitely different from a previous "cigarette cough." There was no hemoptysis.

On physical examination, the blood pressure was 160/80 mm. The patient appeared to be his stated age. There were many senile keratoses. The significant physical findings were limited to the heart and lungs. The heart was normal to percussion and auscultation except for frequent ventricular ectopic beats. On auscultation of the chest, occasional inspiratory wheezes were heard anteriorly over the right chest, particularly over the area of the right middle lobe. There was no limitation of inspiratory excursion. Hemoglobin content of the blood was 14.5 gm. per 100 cc. Erythrocytes numbered 5.3 million per cu. mm. and leukocytes 11,400 per cu. mm. with the cell differential within normal limits. Results of urinalysis were normal. Electrocardiograms were read as within normal limits. The sedimentation rate (Cutler) was normal.

The patient was treated symptomatically and was told to stop smoking, but he did not show any improvement. Fluoroscopic examination showed increased bronchovascular markings in the right middle lobe area and clouding in the right costophrenic sinus area. These observations were substantiated two days later by x-ray examination (Figure 1). At this time, the presumptive diagnosis of a carcinoma of the lung was suggested. (A previous x-ray examination of the chest done elsewhere on December 3, 1948, had shown similar changes of increased bronchovascular markings in the right middle and lower lobes.) Bronchoscopic examination was carried out October 12, 1949, at which time a diagnosis of carcinoma of the lung was made both macroscopically and microscopically (Figure 2). There was a growth in the right main bronchus near the middle lobe orifice, with a 60-degree rotation of the carina. In view of this distortion, and the patient's age, it was felt to be an inoperable lesion.

The patient was symptomatically improved following bronchoscopy and was unwilling to accept therapy until January, 1950. He then was referred for x-ray therapy. Treatment was administered through three 10 x 10 cm. ports aimed at the right hilar area. Anterior, lateral and posterior ports were used and each port received 2,000 r (air). The distance was 50 cm. and the half value layer was 1.7

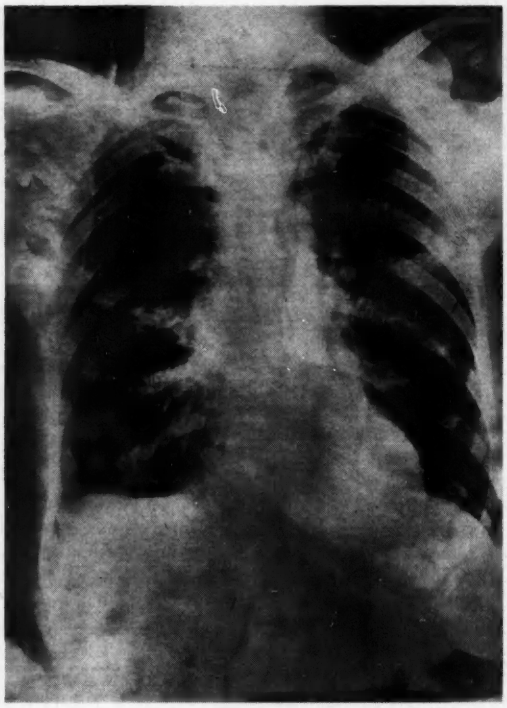

Figure 1.—Initial x-ray film of chest taken October 12, 1949.

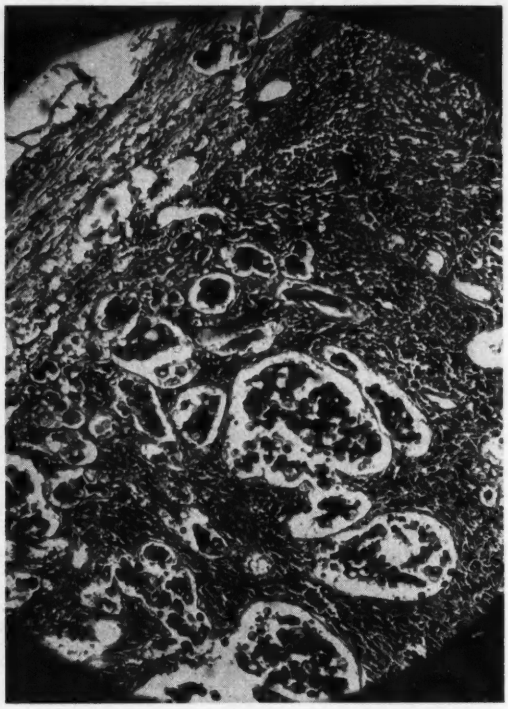

Figure 2.—Photomicrograph of bronchial biopsy tissue, excised October 12, 1949 (×400).

mm., copper. This therapy was given between January 10, 1950, and February 28, 1950. At the end of the course of treatment, the patient complained to his wife about some difficulty in swallowing. Fluoroscopic examination revealed no lesion. Roentgenograms taken on March 3 and April 3, 1950, revealed no essential change in the mass in the right hilar area. However, by June 9, 1950, some decrease in the right hilar mass was noted (Figure 3). By this time the patient was feeling very much better. The cough was less and appetite was improved. In March, 1950, because of a decrease in hemoglobin content to 10.8 gm. per 100 cc. and of erythrocytes to 3.7 million per cu. mm., an infusion of 1,000 cc. of whole blood was given. He temporarily improved, but two more units of whole blood had to be given in June, 1950, at which time digitalization was carried out because of shortness of breath and recurrence of cough.

On September 28, 1950, 11 months after the first bronchoscopic examination, bronchoscopy was done again and only abundant purulent material with no neoplastic cellular constituents was obtained. Symptomatic treatment was given for episodes of syncope, weakness, profuse perspiration, dyspnea and vague abdominal pains often difficult to interpret as to their cardiac or pulmonary origin. At no time did electrocardiograms indicate myocardial infarction and there was presumption that these episodes were

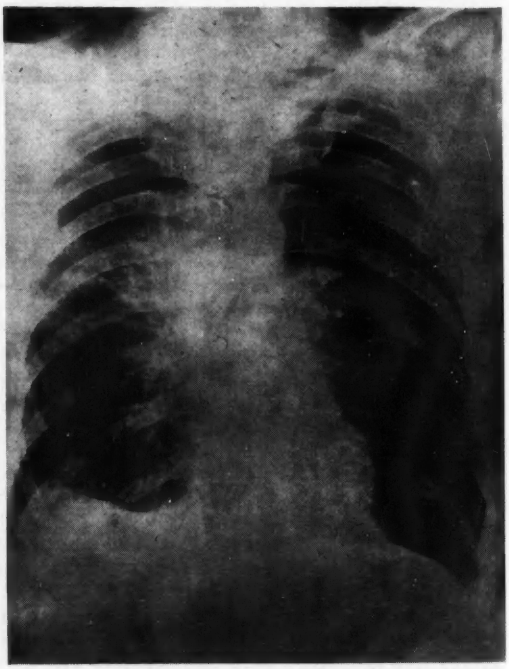

Figure 3.—X-ray film of chest taken June 9, 1950.

on the basis of infection. During this time the cellular contents remained within normal limits. In spite of all of the symptoms from time to time, no significant changes were elicited by repeated physical examination. (From a clinic record about this patient, written by Dr. William W. Newman of San Francisco, in February, 1930, it was learned that the patient at that time had similar complaints as well as evidence of pronounced peripheral arteriosclerosis.)

In July, 1952, bronchoscopic examination was done again and it showed retrobronchial pressure on the right middle lobe bronchus, which was, however, patent. No abnormal cells were observed in material aspirated from the stomach and from the bronchus. It was further noted on fluoroscopic examination at the time that there was some atelectasis of the right middle lobe. In March, 1953, the patient was put in hospital because of dyspnea. The use of positive oxygen pressure with the Bennett valve was attempted without success. On May 18, 1953, x-ray therapy was begun again. During this course, the patient received 1,400 r (air) through a large port to the right anterior chest wall and 600 r (air) through a large port to the right posterior chest wall. The half value layer was 1.0 mm. copper. X-ray therapy was completed on May 29, 1953, and the patient then received 30 mg. of nitrogen mustard intravenously, accompanied by the use of corticotropin (ACTH). An infusion of two units of blood was given about one month later. By August 5, 1953, the patient said that he felt fine. Surprisingly, he remained rather comfortable for the next four months except for some dyspnea on exertion and very mild cough. From December, 1953, until December, 1954, when he died—at the age of 80—the patient had increasing episodes of paroxysms of coughing, dyspnea, vascular collapse and cyanosis, and decreasing activity, physical and mental. The last two months of his life, he was completely bed-ridden. (Figure 4 shows a photograph of the last roentgenogram of the chest.)

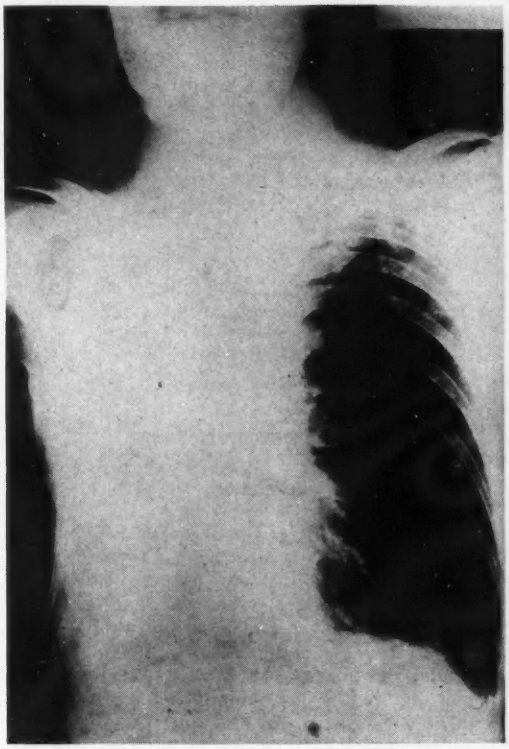

Figure 4.—X-ray film of chest taken September, 1954, showing complete atelectasis of the right lung and shift of the mediastinum.

Pathologist's Report

The pertinent observations at autopsy were reported as follows:

"The body was that of a man appearing in his seventies, small, with general cachexia. The chest cavity was opened, revealing a complete collapse of the right lung down into an approximately 5 cm. nubbin and a complete shift of the mediastinum toward the right with decided compensatory enlargement of the left lung.

"The heart was rather small and sclerotic, with delicate blood vessels throughout, without the slightest suggestion of coronary occlusion. The myocardium was somewhat brownish and softened, but not fibrotic or infarcted. The endocardium was smooth, the valves competent but slightly sclerotic. There was hypertrophy of the right ventricle.

"There was massive compensatory emphysema of the left lung, symmetrical and without particular blebs. Careful search through this lung revealed no metastatic lesion. The right lung was approximately 5 cm. in diameter, completely collapsed, and there was a moderate amount of fibrosis on this side, particularly of the pleura. Very careful search revealed no evidence of metastasis at any point and no evidence of remaining tumor.

"There was a moderate amount of congestion in the liver, but no obvious fibrosis. The gallbladder was present and normal as was the spleen. The kidneys were moderately sclerotic but with a well formed pattern of a moderately old person. The bladder was almost empty and was not inflamed. The stomach showed no dilation. Careful search through it revealed no evidence of tumor, either in it or up and down the retroperitoneal area. The rest of the intestinal tract was almost empty, and no gross abnormalities were observed.

"*Macroscopic diagnosis.* Treated carcinoma of right lung with pulmonary fibrosis and atelectasis; mediastinal shift with massive left pulmonary emphysema.

"*Microscopic description.* Sections through the right lung at the stump of the amputated bronchus and lung showed obvious infiltrations by neoplastic cells (Figure 5). The same neoplastic cells were epithelial, large with abundant cytoplasm,

prominent nuclei and many mitotic figures. Some of the cells were large enough to almost suggest a partial squamous pattern, although actual keratin and pearl formation was not apparent. The right lung showed slight atelectasis and moderate emphysema but no other specific changes or evidence of present inflammation.

"Examination of the liver, adrenal glands, diaphragm and kidneys revealed no significant pathologic changes.

"*Anatomic Diagnosis*

"1. Carcinoma of right lung with radiation therapy with (a) persistence of carcinoma in stump of bronchial area and mediastinal lymph nodes; (b) radiation fibrosis of lung and pleura.

"2. Massive pulmonary emphysema, left side, with shifted mediastinum.

"3. Cor pulmonale and cardiac failure."

DISCUSSION

The original biopsy of the bronchus (obtained at the French Hospital) (Figure 2) was reviewed. This section revealed very small bronchial fragments with a surface epithelium that was quite pleomorphic and mitotically active. One or two points of invasion were noted and there was a striking degree of cellular irregularity. Although the specimen was a small one, it was our opinion that it represented an unequivocal carcinoma, although from the biopsy tissue the degree of invasion or its stage was not apparent. At autopsy, the mediastinal area and radiated lung were quite fibrotic (Figure 5) due to the radiation response, so that it was impossible to discern grossly the neoplasia which was so obviously present on microscopic examination. It was apparent that a carcinoma did exist originally and that it did respond to radiation, although at autopsy there was persistent neoplasm locally and in the regional lymph nodes.

COMMENT

Although this patient required a great deal of careful general medical management, the clinical course leads one to believe that he survived longer than he would have without radiation therapy. He had interludes of months during which he was reasonably comfortable and happy. He lived almost to the age of 80, but his adaptation to the confinement required by this, his first serious illness, was poor. We believe that had the nature of his illness been more clearly understood by him, he would have had an even more favorable response to treatment. For example, he refused several times our suggestions that he receive selective pneumothorax therapy which might have alleviated to some extent the symptoms of complete right lung atelectasis and mediastinal shift. From the autopsy report it seemed that death was owing more to a physiological inability to continue life under the circumstances of the extreme shift of the mediastinum and the advanced emphysema in the functioning lung, than to the carcinoma, which was still localized entirely to the right hilar area.

Figure 5.—Representative section through fibrotic stump of right lung at postmortem examination (×200).

This case report may add evidence to indicate that carcinoma of the lung is not always a hopeless disease as far as therapy is concerned. In particular we feel that the use of radiation therapy for patients with pulmonary tumors that are considered "inoperable" is worth while.

711 D Street, San Rafael (Arons).

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Hazard of Fluid Distention of the Balloon of a Miller-Abbott Tube

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EXTENSIVE AND EFFECTIVE USE has been made of the double lumen Miller-Abbott intestinal tube since it was introduced in 1934.[3]

To our knowledge, however, only three reports of irreversible fluid distention of the balloon have appeared.[1,2,4] In the first,[2] nourishment was introduced through the lumen labeled "Pilling." The substance became caked in the tube, filled the balloon and could not be aspirated. The full balloon ruptured at the cardia during attempted withdrawal of the tube. In the second report,[4] nourishing solution had been introduced into the balloon and at laparotomy was found to be firmly coagulated. In the third report,[1] milkshake feedings were introduced into the balloon and intestinal obstruction developed. Efforts to withdraw the tube were unsuccessful. Upon laparotomy, the balloon was observed to be distended with fluid.

REPORT OF A CASE

The patient was a 42-year-old man who had undergone colectomy with ileoproctostomy for carcinoma of the rectosigmoid and disseminated adenomatosis of the colon.

Figure 1.—One hour after instillation of barium with crescentic flow about distended balloon of Miller-Abbott tube. Tip of tube appears beyond site of obstruction. Five cc. of mercury within 200 cc. of water has assumed spherical shape.

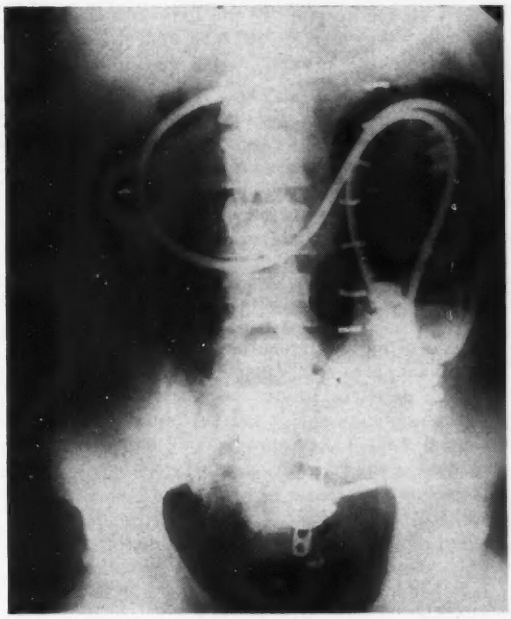

Figure 2.—Six hours after Figure 1, retrograde flow of barium is observed. Spherical shape of mercury persists.

On the sixth postoperative day, a Miller-Abbott tube had to be introduced because of mechanical obstruction of the small bowel. The bowel was decompressed and the patient did well until the eleventh postoperative day, when distention recurred. The position of the spherical mass of mercury remained stationary for two days. An hour after the instillation of barium, a plain film of the abdomen showed a large crescentic shadow of barium at the distal end representing the site of obstruction, with the tip of the tube beyond (Figure 1). Six hours later there was retrograde flow of barium along the tube (Figure 2). The abdomen was reopened on the thirteenth postoperative day because of intractable intestinal obstruction and wound dehiscence. The obstructing balloon of the Miller-Abbott tube was distended with 200 cc. of water. Recovery followed aspiration of this fluid.

A bedside attendant acknowledged putting irrigating water down both lumina for several days before the recurrent obstruction appeared.

DISCUSSION

All personnel rendering bedside care must learn to use this valuable therapeutic tool properly. The orifice to the balloon should be taped and plainly marked to avoid such a potentially serious accident. It would be desirable for the tube to be manufac-

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Submitted August 15, 1957.

tured with the aperture to the balloon at right angles to the long axis of the tube and at least three inches from the proximal open end intended for suction.

Of probable diagnostic significance is the spherical shape of the mercury, representing a surface tension phenomenon in the presence of another fluid. Mercury alone tends to appear as an amorphous mass. Hence, when mercury appears globular, an attempt should be made to aspirate fluid from the balloon.

SUMMARY

A case of intestinal obstruction due to excess fluid in the balloon of the Miller-Abbott tube re-emphasizes the need for proper bedside care to prevent such a complication. It is also suggested that the two proximal ends of the double lumina be more clearly separated at the time of manufacture.

184 Nemaha Street, Pomona (Hauch).

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Torsion and Infarction of the Normal Ovary in Children

L. GORDON FISKE, M.D., Santa Barbara

AN UNUSUAL CAUSE of acute abdominal symptoms in children is torsion with infarction of a normal ovary. Hinshaw and Kugel[4] reported such a case in 1956 and said that 21 cases in all had been reported in the English literature up to that time. However, Baron[1] in 1932 reported a series of 26 cases. Downer and Brines[3] collected reports of 18 cases from the literature and reported a case they had observed. Many of the cases reported in each of these series are of course also included in the others. Baron reported one instance of torsion of the normal ovary, and later torsion and infarction of the remaining ovary in the same patient, necessitating bilateral oophorectomy and salpingectomy.

Although such a condition should possibly be considered in the differential diagnosis of lower abdominal pain, its rarity would put it far down on the list of possibilities. Torsion of the right ovary almost invariably causes clinical symptoms that may be mistaken for those of acute appendicitis, as happened in the case herein reported. Torsion is more common on the right side than on the left. The diagnosis is difficult because of the rarity of tubo-ovarian disease in children. The symptoms of ovarian torsion may simulate those of bowel obstruction or ureteral colic. Rarely is the diagnosis made until exploratory laparotomy is done because of the obviously acute abdominal emergency.

In cases reported previously the clinical features have been similar. At first the pain is cramp-like and not too well localized. Vomiting frequently ensues, and the pain then localizes to either of the lower quadrants of the abdomen and becomes more steady in character. Sometimes a history of previous attacks can be elicited. Upon physical examination, tenderness usually is noted either on the right or left side of the lower abdomen and in some cases other signs of peritoneal irritation are present. There may be radiation of pain to the thigh or genitalia. In several reported cases it was noted that a small, tender pelvic mass was felt on rectal or pelvic examination.

REPORT OF A CASE

A 12-year-old white girl was taken to a physician's office in the early morning of April 28, 1957, because of abdominal pain which had begun 12 hours previously. At first the pain was described as being cramp-like, and not localized. By the time of first examination the pain was beginning to localize to the right lower quadrant and was becoming more steady in character, but with occasional exacerbations. Mild tenderness was noted in the right lower quadrant, but there was no rebound and no rigidity. No masses were felt either abdominally or rectally. The patient did not have fever. Leukocytes numbered 5,000 per cu. mm. and the cell differential was within normal range. No abnormality was noted in the urine.

The family was instructed to bring the child back later in the day for further evaluation, and it was in the late afternoon on her return that surgical consultation was obtained. During the day the pain had become increasingly severe and steady and was more decidedly localized to the right lower quadrant. Vomiting had occurred during the day. The patient had no previous history of digestive distress or symptoms referable to the genitourinary tract. She had had two menstrual periods, the second one having been a week before the present illness. Upon examination the patient appeared to be acutely ill. She tended to lie on her right side with the legs flexed. The temperature was 99.6° F., the pulse rate 100 and respirations 22 per minute. The face was pallid and the skin clammy. There was pronounced right lower quadrant tenderness below McBurney's point, with guarding and mild rigidity. Peristalsis was hypoactive. Upon rectal examination tenderness was

Submitted September 23, 1957.

noted greater on the right, but no masses were felt. The hymen was intact. The impression was very definitely that the patient had acute appendicitis, and she was immediately admitted to the hospital and prepared for operation. At the time of admittance, leukocytes numbered 10,900 per cu. mm.—79 per cent polymorphonuclear cells, 1 per cent eosinophils and 20 per cent lymphocytes. The hemoglobin value and the erythrocyte content were within normal limits. No abnormality was noted in the urine.

A McBurney incision was made. The appendix appeared to be normal but there was a small amount of clear, straw-colored fluid in the lower abdomen. A mass was felt in the cul-de-sac and upon examination it was observed to be the right tube and ovary. The ovary was enlarged to approximately 7x4x3 cm. in diameter. It was dark and edematous and the surface mottled with extravasated black clotted blood. The tube was purple, swollen and edematous. The pedicle was unusually long and was twisted for two complete turns at its base. Immediate resection was considered, but first the pedicle was untwisted and the ovary and tube replaced in the abdomen while the appendix was being removed. Several minutes later they were inspected again, and there was then obviously a return of arterial circulation. The tube was bright red and the ovary, which had diminished in size by about one-third, had taken on a pinkish-white coloration except for the small areas of hemorrhage on the surface. When the surface was nicked in several places, bleeding showed that there had been a return of adequate arterial circulation. It was decided to preserve the ovary and the tubo-ovarian structures were sutured in normal position to the right broad ligament in such a way that torsion could not recur. No complications developed and the patient was discharged from the hospital on the third postoperative day.

COMMENT

Some observers have ascribed torsion of the ovary to unusual length of the pedicle, as in the case herein reported. However, in the case reported by Baron, in which torsion of first one and then the other ovary occurred, the second ovary was noted to have a normal looking pedicle at the time of the first operation. Torsion may be repeated, causing intermittent or recurrent attacks as in the case reported by Hinshaw and Kugel.[4] Torsion causes circulatory stasis, venous occlusion at first, then interruption of arterial flow as torsion progresses. Hemorrhagic infarction finally results.

In ovarian torsion, the right ovary twists clockwise and the left ovary counterclockwise, as viewed with the pedicle pointing away from the observer (Küstner's Law).

It is never possible to state with complete assurance that the adnexae were normal before twisting occurred, because the extensive hemorrhage, necrosis and infarction which follow the twisting would obliterate evidence of any mild inflammation that might be present. Downer and Brines,[3] in reporting upon 19 cases, included only those in which the patient was less than 16 years of age, expressing the thought that under that age venereal disease probably would not be a considerable factor. This limit is doubtless too high, and setting the age limit at 13 years would have reduced the number of cases from 19 to 12—nine in which there was torsion of ovary and tube, two of the ovary only and one of the oviduct only.

Immediate laparotomy with resection of the involved ovary and tube was the method of treatment in other cases reported. In the present case, however, this was deemed unnecessary after a return of circulation was observed when the pedicle was untwisted. It might be well in other cases, therefore, to wait to see if arterial circulation will return, lest the ovary be removed unnecessarily. Since the earlier part of the process is intense venous engorgement, some damage to the ovary may result but if arterial supply is not blocked by thrombosis, a functioning ovary may be preserved. It would seem that in very young girls, ovarian tissue should always be preserved on both sides if feasible, for there is always the possibility that the function of the remaining ovary could be lost later through some disease process.

SUMMARY

Torsion and infarction of the normal ovary and tube is a rare cause of acute abdominal symptoms in children.

The clinical symptoms and signs, if the right uterine adnexa is involved, resemble those of acute appendicitis. Bowel obstruction or ureteral colic may be simulated. Torsion is more common on the right side than on the left. Since left-sided torsion produces a confusing clinical picture not likely to be mistaken for appendicitis, surgical interference is more like to be delayed.

A case of right-sided torsion with early venous infarction is reported. In this case, unlike others previously reported, the ovary and tube were preserved when arterial circulation was observed to be reestablished soon after the pedicle was untwisted. It is suggested that before oophorectomy is done in cases of ovarian torsion untwisting should be done to permit evaluation of arterial sufficiency. Unless irrevocable arterial block has occurred, an otherwise normally functioning ovary may be preserved.

22 West Micheltorena Street, Santa Barbara.

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Endocarditis Following Ventricular Septal Defect Repair

WILLIAM MANDEL, M.D., San Francisco,
M. S. HOFFMAN, M.D., G. H. HEITZMAN, M.D.,
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THE INCIDENCE of endocarditis following operations for repair of congenital or acquired cardiac lesions has been stated to be one per cent.[6] Reports of 30 such cases were found in a review of the literature,[1-6,9-11] although in three of the cases proof of endocarditis was lacking. Herewith is the first reported occurrence of endocarditis following repair of a ventricular septal defect. It is the only known case of endocarditis following approximately 1,200 cardiac operations performed in four hospitals in Denver.

REPORT OF A CASE

A 9-year-old boy was admitted to the National Jewish Hospital in Denver on January 10, 1956, for correction of a ventricular septal defect. He had been in good health until, two years before admission, a febrile illness associated with aching in the joints developed. A cardiac murmur was heard at the time. Several weeks after recovery, the patient noted that he was tired and short of breath oftener than before and could no longer keep pace with his playmates. Questioning brought denial of cough, epistaxis, chest pain, hemoptysis, wheezing, paroxysmal nocturnal dyspnea, ankle edema and cyanosis. The patient was not subject to frequent respiratory infections or sore throats. There was no familial history of congenital cardiac defects.

On physical examination, the patient was observed to be thin and well developed and in no acute distress. The blood pressure was 110/60 mm. of mercury and the pulse rate was 100 per minute. Except for those referable to the cardiovascular system, no abnormalities were noted. There was no clinical evidence of increased venous pressure. The left side of the chest was more prominent than the right and showed active cardiac pulsations. Upon palpation of the precordial region a right parasternal heave and a left ventricular apical thrust were noted. The heart was enlarged to percussion. A systolic thrill was felt over the precordial area, being loudest at the third left interspace near the sternum. The murmur was louder in the fourth than in the first intercostal space. The pulmonic second sound was duplicated and accentuated. The femoral pulsations were felt and there was no edema or cyanosis or clubbing of the extremities.

Results of examination of the blood and the urine were within normal limits. Blood cultures were negative for pathogenic organisms. An electrocardiogram showed evidence of left ventricular hypertrophy, which was confirmed by roentgenographic and fluoroscopic examination. Fluoroscopic examination showed enlargement of the main and branch pulmonary arteries and increased vascularity of the pulmonary parenchyma. Cardiac catheterization was carried out and the results were consistent with the diagnosis of a ventricular septal defect. Blood oxygen saturation was increased three volumes per cent as the catheter passed from the right atrium to the right ventricle. This increase was maintained in the main pulmonary artery. The pressure in the right ventricle was 74/0 mm. of mercury and in the pulmonary artery 72/20 mm. of mercury.

On January 20, by means of hypothermia and coronary artery perfusion, a large ventricular septal defect was repaired under direct vision. The immediate postoperative course was satisfactory, and the patient was ambulatory by the fifth postoperative day. The systolic murmur present before operation was no longer audible. However, on the tenth postoperative day a diastolic murmur, characteristic of that occurring in aortic insufficiency, was heard along the left sternal border. Comparison of a chest roentgenogram with previous films showed a slight increase in the transverse diameter of the heart. Although the patient appeared clinically well, fever that varied between 99° and 100°F. daily developed.

Following the operation, the patient was given 600,000 units of procaine penicillin and 1.0 gram of tetracycline daily. The low grade fever persisted, and on the 24th postoperative day the temperature suddenly rose to a range between 101° and 103°F. This was associated with shaking chills and sweats. Blood cultures grew coagulase-positive staphylococcus aureus sensitive to penicillin, erythromycin and chloramphenicol. Although the antimicrobial therapy was changed to 4,000,000 units of penicillin and 1.0 gram of erythromycin daily, fever persisted. Symptoms and signs of congestive heart failure developed on the thirty-third postoperative day. The patient was treated with digitalis, mercurial diuretics, oxygen, increasing doses of penicillin up to 20,000,000 units daily and chloramphenicol. The blood cultures were negative for organisms after the thirty-seventh postoperative day, but the congestive failure progressed. Dyspnea increased and the patient died on the fifty-sixth postoperative day.

Pathologist's report: At necropsy, passive congestion of all organs, most severe in the liver and lungs, was noted. The subcutaneous tissues were edematous. A loculated right hydrothorax was present. The pericardium and epicardium were thickened and the intervening space was largely obliterated by fibrous adhesions. The heart weighed 385 grams. The right ventricular wall was 8.0 mm. thick; the left ventricle was moderately hyper-

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San Francisco Hospital, San Francisco 10 (Mandel).

trophied. The mitral and tricuspid valves were normal. A completely closed intraventricular septal defect was located high in the membranous portion of the septum. The line of closure of this defect was covered with granulation tissue. Microscopically, this granulation tissue contained Gram-positive cocci. Sinus tracts were found between the sinuses of Valsalva and the main pulmonary artery. The pulmonary artery was dilated and was larger in circumference than the ascending aorta. The pulmonic and aortic valves were normal. The final diagnoses were: Ventricular septal defect surgically repaired; bacterial endocarditis with fistulous tracts secondary to coagulase-positive staphylococcus aureus infection and congestive heart failure, severe.

DISCUSSION

Endocarditis is an uncommon although serious infection after cardiac operations. Koiwai and Nahas[6] reported 12 such cases in a total of 1,190 cardiac operations. Denton and co-workers,[4] in an extension of this series, found 20 instances in a total of 2,263 cardiac operations, an incidence of 1 per cent. We observed only one instance of postoperative endocarditis in approximately 1,200 cardiac operations. Since the majority of cases of endocarditis occurring after cardiac operations are recognized and reported, the incidence of this complication probably lies between 0.1 and 1.0 per cent.

Koiwai and Nahas[7] discussed three possibilities with regard to the bacteremia: The presence of bacteremia before operation, the introduction of the organism at the time of operation and the occurrence of bacteremia following but unrelated to the operation. That the organism is introduced during operation in a majority of cases seems probable in light of the high proportion of cases in which the infecting organism was a staphylococcus resistant to penicillin and other anti-microbial agents. Only two of the reported cases associated with cardiac operation were caused by the streptococcus viridans, the organism that is responsible for 75 to 85 per cent of all cases of endocarditis in general.

Of great importance in endocarditis following cardiac operations is early recognition, followed by intensive treatment. In the present case, as well as in many of the others reported in the literature, the usual symptoms and signs of endocarditis were either absent or masked. The endocarditis may be confused with the postcommissurotomy syndrome, which is also characterized by temperature elevation, by an increase in the erythrocytes and sedimentation rate and by leukocytosis. The diagnosis of the postcommissurotomy syndrome was not seriously considered in any of the reported cases. Larson,[7] in a report on 51 cases of postcommissurotomy syndrome, described one patient who presented a "classical picture of endocarditis." The diagnosis of endocarditis can usually be substantiated by taking frequent blood cultures whenever an unexplained fever occurs in the postoperative period. Early intensive treatment is important because of the high incidence of complications and the high death rate of staphylococcal endocarditis.

The general plan of treatment for staphylococcic endocarditis suggested by Melton and Logue[8] is recommended. As soon as the diagnosis is suspected, 50,000,000 units of penicillin should be given daily by constant intravenous infusion. One to two grams of streptomycin and 2.0 grams of probenecid are given daily. If there is no clinical response by the third day, the dose of penicillin is increased to 100,000,000 units and given for four additional days. As soon as the organism is identified and sensitivity studies reported, other antimicrobial drugs may be employed. Even after clinical improvement begins and blood cultures are negative for the pathogenic organism, treatment is continued with decreased doses of penicillin. The treatment period is usually five to six weeks.

SUMMARY

A case of staphylococcal endocarditis occurring following repair of a ventricular septal defect is presented. This is the thirty-first instance of endocarditis reported complicating cardiac operations, and it is the second instance in which it followed repair of a congenital cardiac lesion. The incidence, source, diagnosis and treatment of this form of endocarditis are briefly discussed.

University of California Service, San Francisco Hospital, San Francisco 10 (Mandel).

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California MEDICAL ASSOCIATION

NOTICES & REPORTS

Council Meeting Minutes

429th Meeting

Tentative Draft: Minutes of the 429th Meeting of the Council, San Francisco, St. Francis Hotel, December 14, 1957.

The meeting was called to order by Chairman Lum in the Georgian Room of the St. Francis Hotel, San Francisco, on Saturday, December 14, 1957, at 9:30 a.m.

Roll Call:

Present were President MacDonald, President-Elect West, Speaker Doyle, Vice-Speaker O'Neill, Secretary Daniels, Editor Wilbur and Councilors MacLaggan, Wheeler, Foster, Wadsworth, Harrington, McPharlin, Sherman, Lum, Bostick, Teall, Kirchner, Reynolds, Varden, Heron, Hoyt and Rosenow. Absent for cause, Councilor Pearman.

A quorum present and acting.

Present by invitation were Messrs. Hunton, Clancy, Thomas and Gillette of C.M.A. staff; Messrs. Hassard and Huber of legal counsel; county society executive secretaries Scheuber of Alameda-Contra Costa, Jensen of Fresno, Marvin of Riverside, Foster of Sacramento, Donmyer of San Bernardino, Nute of San Diego, Neick of San Francisco, Thompson and assistant Pearce of San Joaquin, Wood of San Mateo, Donovan of Santa Clara and DeVere of Stanislaus; Fred O. Field, Los Angeles legal counsel, and Doctors Carl Hadley, Justin J. Stein, Walter E. Batchelder, Matthew N. Hosmer, Jay Ward Smith and Donald M. Campbell.

A special guest during a portion of the meeting was Hon. William F. Knowland, U. S. Senator from California, accompanied by Mr. Arthur F. Strehlow.

1. *Minutes for Approval:*

On motion duly made and seconded, minutes of the 428th Council meeting, held November 10, 1957, were approved.

2. *Membership:*

(a) On motion duly made and seconded, seven delinquent members whose dues had been received since November 10, 1957, were voted reinstatement as active members.

(b) On motion duly made and seconded in each instance, six applicants were voted Retired Membership. These were: Walter L. Bach, Harry C. Fortner, R. D. McBurney, Samuel Rosen, Los Angeles County; F. E. Toomey, San Diego County; D. L. Robertson, Stanislaus County.

(c) On motion duly made and seconded in each instance, six applicants were voted Associate Membership. These were: Don Harper Mills, Los Angeles County; Marilyn F. Hicks, Marin County; G. H. Reifenstein, San Francisco County; Murdo Nicolson, Solano County; Chester Marsh, Sonoma County; Donald A. Ballard, Ventura County.

(d) On motion duly made and seconded in each instance, seven members were voted a reduction of dues because of illness or postgraduate study.

3. *C.M.A. Structural Survey:*

Messrs. Hamilton Wright and William Thompson of Robert Heller & Associates, Cleveland, presented to the Council their report and recommendations following a study of the structure, functions and operations of the Association. Discussion was held

FRANK A. MacDONALD, M.D. . . . . President
FRANCIS E. WEST, M.D. . . . . President-Elect
JAMES C. DOYLE, M.D. . . . . Speaker
J. NORMAN O'NEILL, M.D. . . . . Vice-Speaker
DONALD D. LUM, M.D. . . . . Council Chairman
ALBERT C. DANIELS, M.D. . . . . Secretary-Treasurer
IVAN C. HERON, M.D. . Chairman, Executive Committee
DWIGHT L. WILBUR, M.D. . . . . Editor
JOHN HUNTON . . . . . Executive Secretary
General Office, 450 Sutter Street, San Francisco 8
ED CLANCY . . . . . Director of Public Relations
Southern California Office:
2975 Wilshire Boulevard, Los Angeles 5 • DUnkirk 5-2341

on several recommendations but no positive action taken.

On motion duly made and seconded, it was voted to appoint a special committee consisting of the President, President-Elect, Council chairman and three district councilors to review the report and make recommendations to the next Council meeting on its implementation.

4. *Public Welfare Medical Care:*

Councilor Harrington, chairman of the Council's liaison committee with the State Department of Social Welfare, suggested that members of the House of Delegates be sent several pieces of informational material relative to the public welfare medical care program and that the Council plan to introduce resolutions into the 1958 House of Delegates in connection with this program. On motion duly made and seconded, it was voted to defer action on these proposals until the next Council meeting and that informational material to be chosen by the Executive Committee be assembled for mailing to members of the House of Delegates.

On motion duly made and seconded, the Council voted confidence in the liaison committee, including the chairman and Doctors Samuel R. Sherman, William F. Quinn and John M. Rumsey.

5. *State Bar of California:*

Doctor West, chairman of the committee to cooperate with the State Bar of California, reported that the joint committees of the two organizations had agreed to organize the metropolitan areas initially in the program to provide panels of experts for plaintiffs' attorneys in medical malpractice action. He also reported that an article would be prepared for publication in both medical and law journals to outline the background of this program and report on its progress to date.

6. *Medical Review and Advisory Board:*

Doctor Carl M. Hadley, chairman of the Medical Review and Advisory Board, reported that the jury and hospital studies were progressing and that reports would be available about next June 30. He also reported on the progress of statistical studies and gave a progress report on personnel, finances and other items in the program of the board. It was agreed that Doctor Hadley would bring to a later Council meeting a functional study of the Medical Review and Advisory Board.

7. *Legislative News Service:*

On motion duly made and seconded it was voted to continue subscribing to a Washington legislative news service for those Council members who wished to receive it and to provide the service at cost to those county societies that wanted copies.

8. *Time and Place of Next Meeting:*

It was agreed that the next meeting of the Council would be held in Los Angeles on January 11 and 12, 1958.

Adjournment:

There being no further business to come before it, the meeting was adjourned at 5:15 p.m.

DONALD D. LUM, M.D., *Chairman*
ALBERT C. DANIELS, M.D., *Secretary*

* * *

430th Meeting

Tentative Draft: Minutes of the 430th Meeting of the Council, Los Angeles, Ambassador Hotel, January 11 and 12, 1958.

The meeting was called to order by Chairman Lum in the Colonial Room of the Ambassador Hotel, Los Angeles, on Saturday, January 11, 1958, at 9:30 a.m.

Roll Call:

Present were President MacDonald, President-Elect West, Speaker Doyle, Vice-Speaker O'Neill, Secretary Daniels, Editor Wilbur and Councilors MacLaggan, Wheeler, Foster, Wadsworth, Pearman, Harrington, McPharlin, Sherman, Lum, Bostick, Teall, Kirchner, Varden, Heron, Hoyt and Rosenow. Absent for cause, Councilor Reynolds.

Present by invitation were Messrs. Hunton, Thomas, Clancy, Gillette and Mrs. Griffith of C.M.A. staff; legal counsel Hassard and Huber; county executive secretaries Scheuber of Alameda-Contra Costa, Jensen of Fresno, Geisert of Kern, Bannister of Orange, Marvin of Riverside, Foster of Sacramento, Donmyer of San Bernardino, Nute of San Diego, Neick of San Francisco, Thompson of San Joaquin, Wood of San Mateo and Donovan of Santa Clara; Fred O. Field, legal counsel of the Los Angeles County Medical Association; Ben H. Read of the Public Health League of California; Doctors A. E. Larsen and William Gardenier and Messrs. Etchel Paolini, Richard Lyon and Wilson Wahlberg of California Physicians' Service, and Doctors John Blum, Justin J. Stein, Walter Batchelder and Carl Hadley.

A quorum present and acting.

1. *Minutes for Approval:*

On motion duly made and seconded, minutes of the 429th meeting of the Council, held December 14, 1957, were approved.

2. *Membership:*

(a) A report of membership as of January 8, 1958, was received and ordered filed.

(b) On motion duly made and seconded in each instance, six members were voted Retired Membership. These were: John P. Adams, Paul E. Dolan, Alameda-Contra Costa County; Merl L. Pindell, John C. Webster, Los Angeles County; Max Dunievitz, Placer-Nevada-Sierra County, and C. A. MacDonald, San Bernardino County.

(c) On motion duly made and seconded in each instance, seven applicants were voted Associate Membership. These were: L. V. Foye, Jr., Alameda-Contra Costa County; Samuel Becker, Shelby L. Dietrich, Harry C. Fang, Ernest M. Heimlich, Worth A. Hooper, Stanley N. Rokaw, Los Angeles County.

(d) On motion duly made and seconded, reductions of dues were voted for four members.

3. *Financial:*

(a) A report of bank balances as of January 8, 1958, was received and ordered filed.

(b) A report of income and expenditures for December and the six months ended December 31, 1957, was received and ordered filed.

4. *Committee on Scientific Work:*

On motion duly made and seconded, it was voted to authorize the Committee on Scientific Work to select five guest speakers for each annual session, with the advice of the President and the officers of appropriate scientific sections.

5. *California Physicians' Service:*

Councilor Wadsworth, reporting as a Trustee of California Physicians' Service, reported that studies were under way toward the possibility of converting C.P.S. fee schedules into new schedules based on the Relative Value Studies. He also reported that a new fee schedule was under consideration, which would be based on the Relative Value Studies at a $5 unit factor, to be used on contracts which might be publicly offered.

Doctor Wadsworth also reported that Messrs. Anthon Robertson and K. L. Hamman had terminated their services with C.P.S.

6. *Legal Department:*

Mr. Hassard reported that the State Supreme Court had upheld the decision of the Appellate Court in reversing a lower court finding against a physician in a malpractice case involving points of law of great importance to all physicians.

7. *Committee on Legislation:*

Mr. Hassard reported that a legislative interim committee was discussing the advisability of introducing legislation to provide health and welfare benefits for all state employees.

He also reported that hearings had been held by another interim committee on cancer control legislation. On motion duly made and seconded, it was voted to approve a meeting between the executive and legislative committees of the Association with the directors of the American Cancer Society, California Division, for exploratory purposes on cancer, report to be made to the Council.

Mr. Hassard also reported that another interim committee was considering a proposal to create a State Department of Health with two divisions, one for public health and one for administrative purposes. It was agreed that the Committee on State Medical Services should consider the advisability of the Association's continuing its support of such proposed legislation.

Mr. Ben H. Read, executive secretary of the Public Health League of California, reported that an investigation of the public welfare assistance law would be made by a Legislative Interim Committee. Further discussion was held later.

Mr. Read also reported that one section of the Public Health League of California had urged the reactivation of the United Public Health League for discussions on pending federal legislation. It was agreed that the opinions of the directors of the United Public Health League should be sought on this subject.

On motion duly made and seconded, it was voted that the district councilors should arrange meetings of the delegates in their respective districts for discussions on federal legislation.

7. *Public Welfare Assistance Law:*

Councilor Harrington, chairman of the liaison committee with the State Department of Welfare, discussed the status of the Public Welfare Assistance Law and reviewed resolutions and communications from several county medical societies. It was agreed that all resolutions and statements should be referred to Doctor Harrington's committee and added consultants.

The report of this committee recommended acknowledging receipt of communications from county medical societies in Los Angeles and San Francisco counties, with the statement that the recommendations of these societies were under favorable consideration. On motion duly made and seconded, this was approved.

On motion duly made and seconded, it was voted to send a letter to the entire membership, advising members of the activities of the Association in dealing with this law.

On motion duly made and seconded, it was voted that all mailings to the membership should be on Association stationery and where appropriate should bear the joint signatures of the C.M.A. President and the State Director of Social Welfare.

On motion duly made and seconded, it was voted that legal counsel and consultants should study means of making payments uniform throughout the state under the public welfare assistance law.

8. *Commission on Medical Service:*

Doctor John M. Rumsey, chairman of the Committee on Government-Financed Medical Care Programs, presented a draft of the proposed contract for 1958 under the Medicare Program, negotiations on which will be undertaken in February with the Department of the Army. On motion duly made and seconded, the proposed contract with certain amendments was accepted and the committee authorized to use it, as amended, as a basis for negotiations.

On motion duly made and seconded, it was voted to appoint Doctor Horace Sharrocks of Sonoma County as a member of this committee. The committee is to be split up into three sections, each of which will hereafter concentrate on individual problems in the jurisdiction of the entire committee.

9. *State Department of Public Health:*

Doctor Malcolm H. Merrill, State Director of Public Health, reported that the level of influenza is now at about normal for this time of the year. He also reported that only about two-thirds of Californians under age 40 had received injections of polio vaccine and only about half that number had had more than one injection. In the absence of any further public programs, he stated, the balance of this program must be carried out by private physicians. The incidence of polio in 1957 is the lightest in 20 years, he stated.

Doctor Merrill also reported that revised regulations had now been adopted by the State Board of Health to cover the requirements of the new rabies control law adopted by the 1957 Legislature.

10. *Association Mailing List:*

A request for use of the Association's mailing list was considered and, on motion duly made and seconded, it was voted to deny this and future requests.

10. *Committee on Blood Banks:*

A statement prepared by the Committee on Blood Banks, covering the standards which should apply for any blood bank to secure the sponsorship of the Association, was presented by Doctor Rosenow, chairman of the Commission on Medical Education. On motion duly made and seconded, it was voted to approve this statement of standards and to commend the Committee on Blood Banks for its prompt and effective handling of this subject. This statement of standards reads as follows:

STANDARDS FOR BLOOD BANK SPONSORSHIP BY THE CALIFORNIA MEDICAL ASSOCIATION

1. Blood banks will operate on a nonprofit principle. A copy of the letter of exemption from the United States Bureau of Internal Revenue and the State Franchise Tax Board will be submitted. A letter will be submitted annually by the blood bank president or other responsible officer stating that the blood bank is complying with its nonprofit status. A letter will be submitted annually from the blood bank auditor stating that blood bank funds are not being used for purposes other than that for which the blood bank was formed and that during the past year there have been no substantive changes in the articles of incorporation or the by-laws of the blood bank, except as follows:

2. Blood banks will perform an acceptable community service. Adequate amounts of all types of blood will be supplied to all qualified medical facilities requesting service in the geographic area covered by the individual blood bank at minimum cost to the patient. The method by which this is accomplished is the responsibility of the individual blood bank as long as the basic effort for blood procurement follows the replacement principle.

3. Blood banks will fulfill basic technical standards as outlined by the National Institute of Health and/or the California State Department of Public Health.

4. Each blood bank will be sponsored by the county medical society where it is located. Evidence of such sponsorship will be submitted annually to the C.M.A.

5. The above information will be secured by the C.M.A. Committee on Blood Banks and will be submitted annually to the Council of the C.M.A.

11. *Committee on Postgraduate Activities:*

Doctor Edward C. Rosenow, Jr., chairman of the Committee on Postgraduate Activities, recommended that the committee budget be set to include payments of $500 each, annually, to the participating medical schools as partial reimbursement to them for their overhead expenses in working with the committee. On motion duly made and seconded, this recommendation was approved.

On motion duly made and seconded, it was voted to approve a policy of making postgraduate institutes as nearly self-supporting as possible.

On motion duly made and seconded, it was voted to approve the transfer of the motion picture program at annual sessions from the Committee on Scientific Work to the Committee on Postgraduate Activities.

12. *Committee on Committee Nominations:*

The Chairman, the Council approving, named Councilor Bostick as chairman of the committee to make recommendations for all commission and committee appointments, the other members of his committee to be the chairman of all commissions.

13. *C.M.A. Structural Survey:*

A special committee appointed to review the studies and recommendations made by Robert Heller & Associates on the structure and functions of the Association presented its report through Councilor Sherman, chairman. Other committee members were Doctors MacDonald, West, Lum, Wheeler and Foster.

On motion duly made and seconded, the Council approved the following recommendations:

1. That the Council and administrative office seek to strengthen their liaison with the Woman's Auxiliary and the California Medical Assistants' Association and to work with them in program planning.

2. That the Speaker of the House consider the advisability of distributing the work load of House reference committees equitably, within the terms of existing By-Law provisions, especially that of Reference Committee No. 3, covering new business.

3. That By-Law amendments be prepared to require that resolutions to be presented to the House of Delegates must be submitted at least one month prior to the convening of the House, emergency resolutions to require unanimous approval of the House for later introduction.

4. That district councilors hold at least one meeting each year with the delegates from their Districts, to apprise the delegates about matters of importance before the Council; delegates, in turn, to apprise their district councilors of their thoughts in regard to matters currently under consideration.

5. That the Council make greater use of the headquarters office for studies, analyses, etc., of matters to come before the Council.

6. That one staff member be assigned the sole duty of working with and correlating the activities of all commissions and committees as Director of Commissions and Committees; that the staff member for this appointment at this time be Mr. Robert L. Thomas; and that an additional staff member be employed to take over some of the present duties which Mr. Thomas will necessarily drop in order to undertake his new duties.

It was further agreed that further recommendations of this special committee be taken up at later meetings and that Speaker Doyle be named as an added member of the committee.

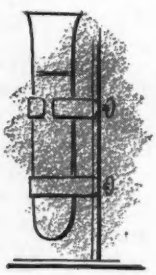
14. *Time and Place of Next Meeting:*

It was agreed that the next meeting of the Council be held on February 8, 1958, in San Francisco.

Adjournment:

There being no further business to come before it, the meeting was adjourned at 5:00 p.m., Sunday, January 12, 1958.

DONALD D. LUM, M.D., *Chairman*
ALBERT C. DANIELS, M.D., *Secretary*



In Memoriam

ALEXANDER, ELMO. Died in Fresno, January 20, 1958, aged 64, of heart disease. Graduate of the University of Texas School of Medicine, Galveston, 1923. Licensed in California in 1925. Doctor Alexander was an associate member of the Tulare County Medical Society.

✤

BRADY, EDWIN HERMS. Died in Auburn, January 8, 1958, of coronary occlusion and decompensation, aged 57. Graduate of Creighton University School of Medicine, Omaha, Nebraska, 1941. Licensed in California in 1948. Doctor Brady was a member of the Placer-Nevada-Sierra County Medical Society.

✤

CAMPBELL, GEORGE M. Died in Glendale, January 18, 1958, aged 47, of uremia. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1935. Licensed in California in 1935. Doctor Campbell was a member of the Los Angeles County Medical Association.

✤

COOPER, ALFRED JOHN. Died January 12, 1958, aged 58. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1925. Licensed in California in 1925. Doctor Cooper was a retired member of the San Diego County Medical Society and the California Medical Association, and an associate member of the American Medical Association.

✤

CRILEY, CLARENCE H. Died in Manhattan Beach, January 14, 1958, aged 76. Graduate of the University of Pennsylvania School of Medicine, Philadelphia, 1907. Licensed in California in 1909. Doctor Criley was a member of the Los Angeles County Medical Association.

✤

DEARING, BRADFORD F. Died in San Francisco, January 5, 1958, aged 67. Graduate of Washington University School of Medicine, St. Louis, Missouri, 1917. Licensed in California in 1920. Doctor Dearing was a member of the San Francisco Medical Society.

HANSON, SAMUEL. Died in Stockton, January 18, 1958, aged 61. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1923. Licensed in California in 1923. Doctor Hanson was a member of the San Joaquin County Medical Society.

✤

LE VALLEY, THOMAS ALEXANDER. Died in North Hollywood, January 1, 1958, aged 51. Graduate of the Tulane University School of Medicine, New Orleans, Louisiana, 1936. Licensed in California in 1937. Doctor LeValley was a member of the Los Angeles County Medical Association.

✤

MCGOWAN, DONALD OSCAR. Died in Carmichael, February 3, 1958, of burns, aged 50. Graduate of the University of Oregon Medical School, Portland, 1934. Licensed in California in 1936. Doctor McGowan was a member of the Sacramento Society for Medical Improvement.

✤

MEADOWS, RUSSELL, JR. Died January 29, 1958, aged 37. Graduate of Northwestern University Medical School, Chicago, 1945. Licensed in California in 1950. Doctor Meadows was a member of the Riverside County Medical Association.

✤

NELSON, HARRY CHARLES. Died in Santa Ana, January 9, 1958, of acute coronary thrombosis, aged 72. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1908. Licensed in California in 1930. Doctor Nelson was a member of the Orange County Medical Association.

✤

STILSON, GEORGE D. Died January 22, 1958, aged 72. Graduate of Cornell University Medical College, New York, N. Y. Licensed in California in 1923. Doctor Stilson was a retired member of the Los Angeles County Medical Association and the California Medical Association and an associate member of the American Medical Association.

Social Security Footnotes

LONG TERM RESULTS of the trend toward Big Pensions and its sponsor Big Government are to be feared. Rewards by government for long life to all the people begins a leveling or averaging process that destroys individuality and initiative. It encourages the welfare state by placing responsibility for a great portion of our people solely in the hands of government.

—From the Department of Public Relations, American Medical Association

REGIONAL POSTGRADUATE INSTITUTE

NORTH COAST COUNTIES

DESCRIPTION OF PROGRAM: In addition to the didactic lectures there will be workshops and question and answer periods in which the physicians will have the opportunity of working in small groups. Workshops in ECG and x-ray interpretation and electrolyte balance will be organized in groups of 10 physicians who will study actual tracings, films and case histories. Small group sessions in which the physicians may submit individual questions in orthopedics and radioisotopes will also be given. Small group sections and workshops will be filled on a first-come—first-served basis. Sign-up sheets for all sections will be available at the Registration Desk. Every effort will be made, however, to schedule additional sections if needed.

Hoberg's Resort, Lake County... April 10–12

PROGRAM

THURSDAY, APRIL 10, 1958

11:00-12:00 and 1:00-1:50 p.m.—Registration

1:50-2:00 p.m.—**Opening Remarks and Introduction**—Alfred A. Thurlow, Jr., M.D.

2:00-2:30 p.m.—**Management of Myocardial Infarction**—George C. Griffith, M.D.

2:30-2:55 p.m.—**Arrhythmias**—Oscar Magidson, M.D., and George C. Griffith, M.D.

3:10-4:00 p.m.—**Panel on Jaundice**

4:00-4:30 p.m.—**Diabetes Mellitus**—Helen E. Martin, M.D.

4:30-5:00 p.m.—**Isotopes**—Franz K. Bauer, M.D.

ELECTIVES: (You may go to one of your choice)

3:10-5:00 p.m.—**Three Sections on Electrocardiography** (limited to 10 students each section)

One Section on Orthopedics (limited to 15)

6:00-7:00 p.m.—Cocktail Hour—Compliments of Hoberg's Resort.

7:00 p.m.—Institute Banquet

FRIDAY, APRIL 11, 1958

9:00-9:55 a.m.—**Surgery in Peripheral Vascular Disease**

9:55-10:50 a.m.—**Newer Diagnostic Tools**—Clyde B. McAuley, M.D.

11:05-11:35 a.m.—**Toxemia of Pregnancy**—Charles F. Langmade, M.D.

11:35-12:05 a.m.—**Office Gynecology**—George A. Macer, M.D.

ELECTIVES: (You may go to one of your choice)

10:00-12:00 a.m.—**Three Sections on Electrocardiography** (limited to 10 each)

12:00-2:00 p.m.—Luncheon

2:00-2:30 p.m.—**Pitfalls in Orthopedics**—Lorin L. Stephens, M.D.

2:30-3:00 p.m.—**Management of Hypertension**—Leonard H. Schwartz, M.D.

3:15-4:30 p.m.—**Panel on Chest Cases**

ELECTIVES: (You may go to one of your choice)

3:15-5:00 p.m.—**Cardiovascular Questions and Answers** (limited to 10)

X-ray Workshop (limited to 10)

Two Sections on Electrolytes (limited to 10)

Cardiac Resuscitation (limited to 15)
Practical experience in Cardiac Resuscitation utilizing dogs

SATURDAY, APRIL 12, 1958

9:00-9:55 a.m.—**Discussion of Medical Case**—Ralph E. Homann, Jr., M.D.

9:55-10:50 a.m.—**Obstetrics and Gynecology**

11:05-12:00 a.m.—**Discussion of Cardiac Cases**—George C. Griffith, M.D.

ELECTIVES: (You may go to one of your choice)

9:00-11:00 a.m.—**Questions and Answers, Isotopes** (limited to 10)

X-ray Workshop (limited to 10)

Cardiac Resuscitation (limited to 15)

OTHER SPECIAL EVENTS:

(1) Continuous Movies

(2) Scientific Exhibits.

HOST: Sonoma County Medical Society . . . **REGIONAL CHAIRMAN:** Alfred A. Thurlow, Jr., M.D., 185 Sotoyome Avenue, Santa Rosa. **Institute Fee:** $20.00. If you have registered for a previous Institute during the 1958 season, fee is $10.00. For additional information, contact Postgraduate Activities office, California Medical Association, 2975 Wilshire Blvd., Los Angeles 5. **All California Medical Association members and their families are cordially invited to attend. Hotel Information:** Special rate of $14.00 (includes 3 meals a day) has been given by Hoberg's Resort. Please make reservations directly with the hotel.

WOMAN'S AUXILIARY
TO THE CALIFORNIA MEDICAL ASSOCIATION

President's Message

THE WIND AND RAIN of winter are now well behind us, and we can look forward to spring and to our annual meeting. It is difficult for me to realize that ten months have elapsed since so many of us last met. What have I done during this time?

To date, I have visited twenty auxiliaries, I've attended the annual convention of the Woman's Auxiliary to the American Medical Association, and I attended the Fall Conference for State Presidents and Presidents-Elect in Chicago. I have covered a good many thousands of miles, I have met several thousands of people; and all are working toward a better tomorrow, by serving American Medicine today.

To assist the California Medical Association in its program for the advancement of medicine and public health is one of our objectives. We are in receipt of a request from the C.M.A. for our help in opposing the Forand Bill which was introduced in August, 1957. As I visit the counties I am agreeably surprised to find the interest that has been provoked by this bill. In a recent visit postal cards were given to all of the members, and before we left all of us had written to our senators and congressmen on why we were opposed to the Forand Bill (H. R. 9467). As a practicing physician, have you written?

To cultivate friendly relations and promote mutual understanding among physicians' families is another of our objectives. This hasn't always been easy. For many years we had a definite "north" and "south." Today this has almost disappeared and we have joined forces in friendship and understanding to participate in any endeavor that will further the cause of American Medicine.

To have the opportunity to visit thirty-four component auxiliaries is a rare and wonderful experience—to visit the large metropolitan city and then the rural areas, and still find physicians' wives acting as the liaison between the profession and the general public. It is the actions of the physician's wife, her community activities, her voluntary services that form the public's opinion of her husband.

Although we are not a fund-raising organization, nevertheless we raise and give away, to some very worthwhile causes, about $50,000 a year. One recipient is our scholarship plan for nurses. Also, some of our auxiliaries maintain a loan fund for needy medical students. Each year we contribute a sizable sum to American Medical Education Foundation and to our own California Physicians' Benevolence.

We are a working community service organization, and health is our concern. If you have ever taken the time to glance over the rosters of the health agencies in your community, you will find many physicians' wives listed; and this is wonderful public relations for the medical profession.

Last summer, as I planned my year ahead, I was concerned with, "What will my message be as I tour about?" I can't begin to tell you how many people I asked; and, as with much in life, I had to solve this myself. It all became very simple one day. I had a request from Ventura County. The president asked, "When you visit our Auxiliary, would it fit your plans to include in your talk an explanation of the aims and functions of the American Medical Association?"

Further, to quote Mrs. James Moore, "Your theme is to 'inform your membership' and that same theme is one of our own county's primary objectives this year. And, of course, you have said your intention is to please the counties." This was my answer, and every month I write ahead and ask the county president if she has a topic she would like me to discuss. This has indeed been a valuable experience for me and, I hope, for the different county memberships.

I'm only sorry that many members cannot experience this opportunity to visit and know the extent of the work as done by thirty-four auxiliaries in California; together we serve the nation's largest Auxiliary.

MRS. LEONARD D. OFFIELD
President, Woman's Auxiliary to the California Medical Association

NEWS & NOTES

NATIONAL • STATE • COUNTY

ALAMEDA

The seventh annual **Clifford D. Sweet Seminar,** sponsored by Children's Hospital of the East Bay, will be held May 16 and 17 at the Claremont Hotel in Berkeley.

The guest speakers will be Dr. James G. Hughes, professor of pediatrics and chairman of the Department of Pediatrics, University of Tennessee Medical School, and Dr. Paul H. Holinger, professor of broncho-esophagology, University of Illinois and Children's Memorial Hospital.

LOS ANGELES

Dr. Ross Golden, visiting professor of radiology at the University of California at Los Angeles School of Medicine, was presented with the American College of Radiology's gold medal at the recent annual meeting of the college in Chicago. Dr. Golden became the nineteenth recipient of the gold medal, which is given for outstanding service in radiology, in the almost 40-year history of the college. Dr. Lowell Goin of Los Angeles, a former winner of the honor, took part in the presentation ceremonies.

* * *

The annual meeting of the **California Academy of Preventive Medicine** will be held at 6:00 p.m., Wednesday, April 30, 1958, in the Regency Room of the Ambassador Hotel, following the Public Health Section meeting.

There will be a social hour, dinner, a nationally known speaker for the scientific section, and a short business session, the academy announced. Members of the American College of Preventive Medicine and Diplomates of the American Board of Preventive Medicine are invited to participate. Physicians planning to attend may write to L. S. Goerke, M.D., University of California at Los Angeles Medical Center, Los Angeles 24.

* * *

The American College of Chest Physicians, California Chapter, will hold a scientific meeting, Saturday, April 26, from 9:00 a.m. to 5:00 p.m. in the Embassy Room, Ambassador Hotel, Los Angeles. A luncheon and business meeting will be held at 12:30 in the Embassy Room.

SAN FRANCISCO

The annual **Memorial Staff Day of St. Mary's Hospital** will be held this year on Wednesday, April 16, 1958, from 9 a.m. to 4 p.m. in the hospital auditorium. Occlusive Vascular Disease will be the main topic of the meeting, with Dr. Denton Cooley of Baylor Medical School, Houston, presenting the surgical aspects, the medical views being given by his guest confreres. Dr. Cooley also will participate with his confreres in a clinical-pathological conference with St. Mary's staff members and their guests. Original papers by staff members will complete the agenda. The day will be terminated by a dinner in the Gold Room of the Fairmont Hotel. The meeting is open to all members of the profession. Information may be obtained from Miss Marguerite Hancock at St. Mary's Hospital.

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A symposium to demonstrate **treating cleft lip and palate** by means of group management is scheduled by the Plastic and Reconstructive Surgery Center of Saint Francis Hospital, San Francisco, for April 21 and 22. It will be held in the hospital and is open to all who are interested in corrective methods for deformity of this type.

Guest speakers will be four specialists from the University of Illinois who have outstanding experience in this type of treatment. They are Herbert R. Kobes, M.D., director, Division of Services for Crippled Children, State of Illinois; Herbert Koepp-Baker, Ph.D., director of the Cleft Palate Center; Edward F. Lis, M.D., associate professor of pediatrics, College of Medicine, and director of the Center for Handicapped Children; and Samuel Pruzansky, D.D.S., associate professor of orthodontics, College of Dentistry, and associate director of the Cleft Palate Training Program.

For the past three and a half years, the Plastic and Reconstructive Surgery Center of Saint Francis Memorial Hospital has conducted a monthly conference in which surgeons meet with orthodontists, speech therapists, otorhinolaryngologists and pediatricians to consider the problems of cleft palate patients.

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A teaching exhibit from the University of California Medical Center in San Francisco was awarded the **Clyde L. Cummer Gold Medal** of the American Academy of Dermatology and Syphilology.

The Cummer Medal is awarded annually by the academy for an exhibit of high teaching value. The University of California exhibit used color transparencies, drawings and text to describe the skin disorders and other medical problems of leg amputees. It was shown at the academy's recent Chicago meeting.

The exhibit was prepared by the staff of the Biomechanics Laboratory at the University of California Medical Center under the supervision of Dr. Verne T. Inman, professor of orthopedic surgery, and Dr. Henry E. Loon, medical coordinator of the laboratory. Panels on skin disorders frequently troublesome to amputees were prepared by Dr. S. William Levy, assistant clinical professor of dermatology, and Dr. Gilbert H. Barnes, clinical instructor in dermatology.

GENERAL

Dr. Charles E. Smith of Berkeley and **Dr. Dave F. Dozier** of Sacramento were appointed by Governor Goodwin J. Knight to the State Board of Public Health for new terms ending January 15, 1962.

Dr. Smith, dean of the University of California School of Public Health, was originally appointed to the board in 1940 and is currently serving as president of the board. Dr. Dozier was originally appointed in 1956.

No. 1 Killer—The leading cause of hospitalization in the Air Force is not air crashes but automobile accidents.

POSTGRADUATE EDUCATION NOTICES

THIS BULLETIN of the dates of postgraduate education programs and the meetings of various medical organizations in California is supplied by the Committee on Postgraduate Activities of the California Medical Association. In order that they may be listed here, please send communications relating to your future medical or surgical programs to: Mrs. Margaret H. Griffith, Director, Postgraduate Activities, California Medical Association, 2975 Wilshire Boulevard, Los Angeles 5.

UNIVERSITY OF CALIFORNIA AT LOS ANGELES

The Clinical Approach to Diseases of the Blood. Wednesday, March 19. Six hours. Fee: $25.00.

Dermatology in General Practice (to be limited to 20), Wednesdays, April 2 to May 7. Twelve hours.†

Medical Technology Workshop: Hematology. Saturday and Sunday, April 12 and 13. Six hours. Fee: $8.00.

Proctology. Wednesday, April 16. Six hours.†

Advances in Behavioral Science of Significance for Rehabilitation. Saturday, April 26. Six and three-quarters hours. Fee: $10.00.

Casts, Splints and Bandages. Wednesday, May 7. Seven hours.†

Collagen Diseases. Friday and Saturday, May 23 and 24. Nine hours. Fee: $30.00.

Emotional Problems in Office Practice (University of California Residential Conference Center, Lake Arrowhead). Thursday through Saturday, June 5 to 7. Twelve hours.†

Seventh Annual Symposium on Medical Technology. Saturday and Sunday, June 14 and 15. Twelve hours. Fee: $20.00.

Techniques of Hypnosis (Limited to 40). Monday through Wednesday, June 16 to 18. Fifteen hours. Fee: $65.00.

Advanced Techniques and Application of Hypnosis (Limited to 25). Wednesday through Friday, June 18 to 20. Fifteen hours. Fee: $110.00.

Techniques of Surgery. Monday through Friday (limited to 14), July 28 to August 1. Thirty-five hours.†

Internal Medicine (at University of California Residential Conference Center, Lake Arrowhead), Wednesday through Saturday, August 20 to 23. Twelve hours.†

Surgical Anatomy (Dissection). Friday and Saturday. Date to be announced. Six hours.†

Obstetrics and Gynecology. Date, hours and fee to be announced.

Surgery of Trauma. Date, hours and fee to be announced.

Contact: Thomas H. Sternberg, M.D., Assistant Dean for Postgraduate Medical Education, U.C.L.A., Los Angeles 24. BRadshaw 2-8911, Ext. 202.

†Fee to be announced.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

Children's Hospital Medical Seminar on Allergies. Saturday, March 29. Seven hours. Fee: $12.50.

Diagnostic Radiology. Saturday through Wednesday, March 29 to April 2. Thirty-five hours. Fee: $75.00.

Ear-Nose-Throat. Friday and Saturday, June 6 and 7. Fourteen hours. Fee: $40.00.

Interpretation of Laboratory Tests. Date, hours and fee to be announced.

Fundamental Principles of Radioactivity and the Diagnostic and Therapeutic Uses of Radioisotopes. Two or three month course limited to one enrollee per month. Per month, $250.00.

Contact: Seymour M. Farber, M.D., Head, Postgraduate Instruction, Office of Medical Extension, University of California Medical Center, San Francisco 22. MOntrose 4-3600, Ext. 665.

STANFORD UNIVERSITY SCHOOL OF MEDICINE

Morning Clinical Conferences, each Monday, Room 515. *Contact:* D. H. Pischel, M.D., Professor, Division of Ophthalmology, Stanford University School of Medicine, 2398 Sacramento St., San Francisco 15.

Postgraduate Conference in the Surgery of Trauma. March 24 to 28.

Postgraduate Conference in Ophthalmology. March 31 to April 4.

UNIVERSITY OF SOUTHERN CALIFORNIA, LOS ANGELES

Cardiac Resuscitation. Sponsored by the Los Angeles County Heart Association each Wednesday throughout the year, 4 to 6 p.m. Residents admitted without fee. Tuition for all other physicians: $30.00. (Each session all-inclusive.)

Basic Home Course in Electrocardiography. One year Postgraduate Series, electrocardiogram interpretation by mail. Physicians may register at any time and receive all 52 issues. Fifty-two weeks. Fee: $100.00.

Advance Home Course in Electrocardiography. One year postgraduate series, electrocardiogram interpretation by mail. Fifty-two issues: $85.00. Physicians may register at any time.

Edematous States. Emphasis placed on understanding of the basic principles involved in edema formation and their relationship to clinical problems. March 28 and 29, Hotel Statler, Los Angeles. Tuition: $56.00.

Problems of Malpractice. Lectures will be presented on problems relating to malpractice situation in California, May 17, Hotel Statler, Los Angeles. Tuition: $18.00.

Office Orthopedics. Designed to be of value to the physician in general practice. May 23 to 25, Hotel Statler, Los Angeles, 9 to 5 each day. Fee: $75.00.

Special Announcement: From August 5 to August 21, 1958, the University of Southern California School of Medicine will hold a postgraduate course in Honolulu and on board the *S.S. Matsonia.* The course will center around actual case histories, which will be used to emphasize diagnostic and therapeutic features.

Contact: Phil R. Manning, M.D., Director, Postgraduate Division, University of Southern California School of Medicine, 2025 Zonal Avenue, Los Angeles 33. CApital 5-1511.

COLLEGE OF MEDICAL EVANGELISTS

Vue-Vox Postgraduate Refresher Courses. Courses are made up of four or more half-hour lectures each, recorded on hi-fi magnetic tape and illustrated by 35-mm. filmstrips or slides in full color, and adapted for use on any standard tape recorder and filmstrip or slide projector, automatic or manual.

Contact: Paul D. Foster, M.D., chairman, Committee on Audio-Visual Courses, College of Medical Evangelists School of Medicine, 316 North Bailey St., Los Angeles 33.

CALIFORNIA MEDICAL ASSOCIATION POSTGRADUATE COURSES

POSTGRADUATE INSTITUTES—1958

SAN JOAQUIN VALLEY COUNTIES, in cooperation with Stanford University School of Medicine, Hotel Californian, Fresno, March 20 and 21, 1958. Chairman: Henry L. Tiesche, M.D., 1759 Fulton St., Fresno.

NORTH COAST COUNTIES, in cooperation with USC School of Medicine, Hoberg's Resort, Lake County, April 10, 11 and 12, 1958. Chairman: Alfred A. Thurlow, Jr., M.D., 185 Sotoyome Ave., Santa Rosa.

Contact: One of the chairmen listed above, or Mrs. Margaret H. Griffith, Director, Postgraduate Activities, California Medical Association, 2975 Wilshire Blvd., Los Angeles 5. DUnkirk 5-2341.

Postgraduate Courses during California Medical Association Annual Meeting

Abdominal Pain. Program by U.C.L.A. School of Medicine. April 28, 29, 30, 9:00-12:00 a.m. Ambassador Hotel, Los Angeles.

Management of Trauma. Program by College of Medical Evangelists. April 28, 29, 30, 9:00-12:00 a.m. Ambassador Hotel, Los Angeles.

Liver Diseases. Program by U.S.C. School of Medicine. April 27, 2:00-5:00 p.m., Los Angeles County General Hospital, and April 28-29, 9:00-12:00 a.m., Ambassador Hotel, Los Angeles.

Guest Speakers: William A. Altemeier, M.D., University of Cincinnati School of Medicine; Charles S. Davidson, M.D., Harvard Medical School; Mark M. Ravitch, M.D., Johns Hopkins University School of Medicine; Bronson S. Ray, M.D., Cornell University Medical College.

Fee: $25.00 each course

For additional information and complete program write: Postgraduate Activities, California Medical Association, 2975 Wilshire Boulevard, Los Angeles 5.

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AUDIO DIGEST FOUNDATION, a nonprofit subsidiary of the C.M.A., now offers (on a subscription basis) a series of hour-long tape recordings designed to keep the physician abreast of current happenings in his particular field. Composed of practice-useful abstracts from 600 leading journals, with short lectures and editorial comments from prominent physicians, Audio Digest offers programs covering general practice, surgery, internal medicine, obstetrics and gynecology, and pediatrics.

Contact: Claron L. Oakley, editor, 1919 Wilshire Blvd., Los Angeles 57.

Medical Dates Bulletin

MARCH MEETINGS

CALIFORNIA SOCIETY OF PLASTIC SURGEONS Annual Meeting, March 20 to 22, Del Monte Lodge, Del Monte, California. *Contact:* Benjamin F. Edwards, M.D., 2200 Santa Monica Blvd., Santa Monica.

AMERICAN COLLEGE HEALTH ASSOCIATION Annual Meeting, March 25 to 29, Ambassador Hotel, Los Angeles. *Contact:* Donald McKinnon, M.D., Student Health Service, University of California Medical Center, Los Angeles 24.

SANTA CLARA AND SAN MATEO COUNTY HEART ASSOCIATIONS Second Annual Postgraduate Symposium on Heart Disease, March 26. Stanford Campus, Palo Alto, 9 to 5. Fee: $5.00. *Contact:* John Blum, Executive Director, San Mateo County Heart Association, 181 Second Avenue, San Mateo; or Mrs. Ruth West, executive director, Santa Clara County Heart Association, 461 Porter Building, San Jose.

APRIL MEETINGS

SAN FRANCISCO HEART ASSOCIATION Nurses Institute on the Care of the Cardiac Patient, April 2 and 3. Marina Junior High School, San Francisco, 8:30 a.m. to 4:00 p.m. *Contact:* Miss Jean Sullivan, program director, 259 Geary St., San Francisco.

CANCER COMMISSION, CALIFORNIA MEDICAL ASSOCIATION CANCER CONFERENCE for Imperial County Medical Society, April 8, Pioneers Memorial Hospital, Brawley.*

CALIFORNIA TUBERCULOSIS AND HEALTH ASSOCIATION, CALIFORNIA TRUDEAU SOCIETY and the CALIFORNIA CONFERENCE OF TUBERCULOSIS WORKERS Annual Meeting, Villa Hotel, San Mateo, April 10 through 12, 1958. *Contact:* E. L. Daggett, director public information, 130 Hayes Street, San Francisco 2, HEmlock 1-8771.

VALLEY CHILDREN'S HOSPITAL Spring Clinics, April 11 and 12. Roosevelt High School Auditorium, Fresno. *Contact:* Valley Children's Hospital, Fresno.

ANESTHESIA SECTION, LOS ANGELES COUNTY MEDICAL ASSOCIATION Third Annual Spring Postgraduate Meetings at LACMA headquarters, April 12 and 13. *Contact:* Thomas W. McIntosh, M.D., chairman, 686 E. Union Street, Pasadena.

CANCER COMMISSION, CALIFORNIA MEDICAL ASSOCIATION CANCER CONFERENCE for Kern County Medical Society, April 15, El Tejon Hotel, Bakersfield.*

AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS, April 21 to 23, Los Angeles. *Contact:* John C. Ullery, M.D., secretary, 15 South Clark St., Chicago 3.

CANCER COMMISSION, CALIFORNIA MEDICAL ASSOCIATION CANCER CONFERENCE for Mendocino-Lake County Medical Societies, April 24, State Hospital, Ukiah.*

AMERICAN COLLEGE OF CHEST PHYSICIANS, California Chapter, Scientific Meeting, April 26, 9 to 5, Embassy Room, Ambassador Hotel, Los Angeles. *Contact:* Thomas B. Wiper, M.D., secretary-treasurer, 536 Mason Street, San Francisco 2.

**Contacts:* Walter E. Batchelder, M.D., medical director, California Medical Association Cancer Commission, 450 Sutter St., San Francisco 8.

AMERICAN SOCIETY OF INTERNAL MEDICINE Annual Meeting, Chalfonte-Haddon Hall, Atlantic City, April 26 and 27. *Contact:* Mrs. Mildred B. Coleman, assistant secretary, or Claude P. Callaway, M.D., secretary-treasurer, 350 Post Street, San Francisco.

CANCER COMMISSION, CALIFORNIA MEDICAL ASSOCIATION PRE-CONVENTION CONFERENCES on Pathology and Radiology, April 26, Ambassador Hotel, Los Angeles.*

CALIFORNIA MEDICAL ASSOCIATION Annual Meeting, Ambassador Hotel, Los Angeles, April 27 to 30. *Contact:* John Hunton, executive secretary, 450 Sutter St., San Francisco 8, or Ed Clancy, director, Public Relations, 2975 Wilshire Blvd., Los Angeles 5.

MAY MEETINGS

LOS ANGELES COUNTY HEART ASSOCIATION Annual Membership Meeting, May 1, 7:00 p.m., Los Angeles. *Contact:* Chauncey A. Alexander, executive director, 660 S. Western Avenue, Los Angeles 5.

CALIFORNIA CONFERENCE OF LOCAL HEALTH OFFICERS Semi-Annual Meeting, Los Angeles, May 1 and 2. *Contact:* Dr. John C. Dement, chief, Division of Local Health Service, State Department of Public Health, 2151 Berkeley Way, Berkeley 4.

WESTERN GERONTOLOGICAL SOCIETY Third Annual Convention, May 3 and 4, Hotel Statler, Los Angeles. Begins 1:00 p.m. May 3. *Contact:* Chas. A. Preuss, M.D., president, 1317 Santa Barbara Street, Santa Barbara.

GROUP PSYCHOTHERAPY ASSOCIATION OF SOUTHERN CALIFORNIA Annual Meeting, May 3, all day, Chapman Park Hotel, Los Angeles. *Contact:* E. Parl Welch, Ph.D., 450 N. Bedford Drive, Beverly Hills.

CANCER COMMISSION, CALIFORNIA MEDICAL ASSOCIATION CANCER CONFERENCE for Sonoma County Medical Society, Santa Rosa, May 8.*

AMERICAN PSYCHIATRIC ASSOCIATION Annual Meeting, May 12 to 16, Civic Auditorium, San Francisco. *Contact:* Alfred Auerback, M.D., 450 Sutter St., San Francisco.

HAWAIIAN DIVISIONAL MEETING, AMERICAN PSYCHIATRIC ASSOCIATION, May 17 to 22, Hawaiian Village, Honolulu. *Contact:* Alfred Auerback, M.D., 450 Sutter St., San Francisco.

WESTERN BRANCH, AMERICAN PUBLIC HEALTH ASSOCIATION Annual Meeting with Canadian Public Health Association, May 19 to 23, Vancouver, B. C. *Contact:* Mrs. L. Amy Darter, secretary-treasurer, 2151 Berkeley Way, Berkeley 4.

AMERICAN LARYNGOLOGICAL ASSOCIATION, May 19 to 20, San Francisco. *Contact:* James H. Maxwell, M.D., secretary, University Hospital, Ann Arbor, Michigan.

AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION, May 21 to 23, San Francisco. *Contact:* F. Johnson Putney, M.D., secretary, 1719 Rittenhouse Square, Philadelphia, Pa.

CALIFORNIA HEART ASSOCIATION Annual Meeting, Scientific Session and Directors Meeting, Hacienda Motel, Fresno, May 23 to 25. *Contact:* J. Keith Thwaites, executive director, 1428 Bush St., San Francisco.

SUMMER AND FALL MEETINGS

AMERICAN COLLEGE OF CHEST PHYSICIANS 24th Annual Meeting, June 18 to 22, San Francisco. *Contact:* Mr. Murray Kornfeld, executive director, 112 East Chestnut St., Chicago 11, Ill.

AMERICAN MEDICAL ASSOCIATION Annual Meeting, June 23 to 27, San Francisco. *Contact:* American Medical Association, 535 North Dearborn St., Chicago 10.

AMERICAN PROCTOLOGIC SOCIETY, June 29 to July 3, Los Angeles. *Contact:* Norman D. Nigro, M.D., secretary, 10 Peterboro St., Detroit 1, Michigan.

IDAHO STATE MEDICAL ASSOCIATION Annual Convention, July 6 to 9, Sun Valley, Idaho. *Contact:* Armand L. Bird, executive secretary, 364 Sonna Building, Boise.

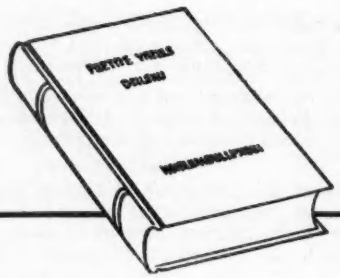
WASHINGTON STATE MEDICAL ASSOCIATION Annual Convention, September 14 to 17, 1958, Spokane, Washington. *Contact:* Ralph W. Neill, executive secretary, 1309 Seventh Ave., Seattle, Wash.

CALIFORNIA ACADEMY OF GENERAL PRACTICE Tenth Annual Scientific Assembly, October 5 to 8, Masonic Temple, San Francisco. *Contact:* William W. Rogers, executive secretary, 461 Market Street, San Francisco 5.

LOS ANGELES COUNTY HEART ASSOCIATION Professional Symposium, October 8 and 9, Wilshire Ebell Theatre, 9 to 5. *Contact:* C. A. Alexander, executive director, Los Angeles County Heart Association, 660 S. Western Avenue, Los Angeles 5.

CALIFORNIA SOCIETY OF INTERNAL MEDICINE Annual Meeting, October 17 to 19, Ahwahnee Hotel, Yosemite. *Contact:* Mrs. Mildred B. Coleman, executive secretary, or Dr. Clyde C. Greene, secretary-treasurer, 350 Post St., San Francisco 8.

AMERICAN HEART ASSOCIATION Scientific Sessions and Meetings, October 24 to 28, Fairmont Hotel and Civic Auditorium, San Francisco. *Contact:* J. Keith Thwaites, executive director, California Heart Association, 1428 Bush Street, San Francisco 9.



THE PHYSICIAN'S *Bookshelf*

CURRENT SURGICAL MANAGEMENT—A Book of Alternative Viewpoints on Controversial Surgical Problems—Editors: John H. Mulholland, M.D., New York University College of Medicine, Editor-in Chief; Edwin H. Ellison, M.D., Ohio State University College of Medicine, and Stanley R. Friesen, M.D., University of Kansas Medical Center. With Contributions by 76 American Authorities. W. B. Saunders Company, Philadelphia, 1957. 494 pages, $10.00.

This is an interesting book which is directed towards the practicing surgeon, not the student or intern. It will be of particular interest to residents in surgical training who are anxious to have alternative viewpoints about surgical problems of controversial nature presented with strong and equal conviction though expressing opposing viewpoints. Each controversial area is discussed first by a prominent experienced surgeon expressing one view of surgical therapy, and immediately thereafter the next chapter presents an alternative surgical viewpoint by another expert with equal logic and vigor. The controversial areas discussed cover such topics as gastrointestinal bleeding, peptic ulcer, portal hypertension, carcinoma of the breast, cholecystitis, thyroid carcinoma, and other similar subjects.

The discussions are pointed, concise, and written by prominent surgeons of wide experience. The divergent views point up the fact that answers to the problems under discussion of true significance and value can only be obtained by subjecting the problems to designed and controlled experimentation. The scientific method must be applied to clinical experiments in the future if the answer is to represent other than strong personal convictions based upon personal experience in surgery. Design and control of clinical research might yield better answers to these basic surgical problems, but the book makes an honest effort to present the alternative viewpoints with equal candor and conviction.

This book is valuable and enjoyable reading for the surgeon, and may stimulate designed experiments of a clinical nature to yield more scientific answers to basic surgical questions.

VICTOR RICHARDS, M.D.

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DERMATOLOGIC FORMULARY—Frances Pascher, M.D., Editor, Hoeber-Harper, New York, 1957. 172 pages, $4.00.

In its preface this book notes that one of its main purposes is to serve the practitioner by listing the most tried and useful dermatologic prescriptions. Another objective is to supply a model dermatologic formulary from which other hospitals, clinics and institutions can select a longer or shorter list of standard preparations for the treatment of skin diseases. In selecting the individual items thought was given to the stability, the sensitizing potential, the pH, the availability, the practical "consumer acceptance," and the cost, as well as to the efficacy of the drug.

Each preparation is listed by name and number. Its formula is given and its chemistry and properties are briefly described. A short and simple discussion of each is then given under the headings of Actions and Uses, Indications, Contraindications and Directions. In some cases additional notes are provided under the headings of Side Effects and Caution.

The book is divided into four sections—Topical Remedies, Systemic Therapy, Articles for Clinic Use and Therapeutic Aids. The major part of the book is devoted to the first two sections. In Section I topical remedies are described under the headings of baths, soaps, shampoos, wet dressings, lotions, ointments, powders, lozenges and the like. In Section II subdivisions of systemic therapy include acids and antacids, analgesics, antibiotics, antihistamines, hormones, and so forth. In Section III listings include local anesthetics, biologicals, cauterizing agents, dressings and bandages and other miscellaneous preparations. Section IV contains cosmetic and treatment aids, directions for long-term corticotropin and/or corticosteroid therapy, and outlines printed instructions for patients' use in care of acne, impetigo and other pyodermas, scabies, home care of scalp ringworm, varicose veins and wet dressings.

In all, more than 250 individual preparations or therapeutic aids are listed. The index is comprehensive. The drugs or compounds are listed alphabetically. The dermatoses or skin conditions are also listed. One can, therefore, refer to the index either for suggestions regarding choice of treatment for a disease, or for a description of the properties and use of a given drug.

I believe this book serves its purposes very well. It should be useful both to individual practitioners who treat skin diseases and to hospitals and clinics as a model for their dermatologic formularies.

HERMAN V. ALLINGTON, M.D.

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PRACTICAL ELECTROCARDIOGRAPHY—Second Edition—Henry J. L. Marriott, M.D., Associate Professor of Medicine, University of Maryland. The Williams and Wilkins Company, Baltimore, 1957. 226 pages, $5.00.

Dr. Marriott's text book is a clear, simple, lucid account of electrocardiography for beginners. The illustrations are good, the material is up-to-date, and the book is very easy to read. The salient diagnostic features of each pattern are clearly indicated in block summaries which facilitates the reading. There is a short, but pertinent, bibliography at the end of each chapter.

The discussion of each subject is brief and elementary and will not appeal to advanced students. The account of congenital heart disease is inadequate because of its extreme brevity. Physiological and electrophysiological discussions are exceedingly limited.

The book can be recommended as an elementary primer for individuals who would like a sound summary of electrocardiographic patterns for review. It is not recommended for specialists in the field.

PROBLEMS IN AMOEBIASIS—Charles William Rees, Ph.D. Charles C. Thomas, Springfield, Illinois, x+119 pages. 1955. $4.75.

Dr. Rees has led a productive career in investigations in parasitic protozoa. For twenty years he was associated with the National Institutes of Health, studying *Entamoeba*. Upon retirement from the N.I.H., he became head of research on amoebiasis at Northwestern School of Medicine in Chicago. His book Problems in Amoebiasis brings together in a concise manner the current status of basic information on the problem.

The history of *Entamoeba* is divided into three periods. In the first there were doubts that it caused dysentery; in the second it was regarded as an absolute pathogen; and in the third and current period there is a wide discrepancy of opinion among the workers.

Because of the little information available on the inherent pathogenicity of *E. histolytica*, its method of attack, or its participation with other microorganisms in the production of amoebiasis, only limited progress has been made in chemotherapy.

Although practical approaches such as sanitation, filtration and clinical treatment of water, sewage disposal, inspection of handling and processing of food, screening of buildings against flies, and popular education have greatly reduced the incidence of *E. histolytica*, the basic problems in amoebiasis now are in the fields of physiological chemistry, bacteriology, and clinical medicine.

Present day methods of diagnosis of *Entamoeba* infections at best require skill, experience, and patience. The author, through his years of experience, ably discusses needs for caution in handling feces and gives three methods of procedure, results, and their interpretation. They include (1) microscopic examination with special emphasis on the zinc flotation method, including a discussion on its use, (2) "in vitro" cultures, using antibiotics to inhibit bacterial growth, and (3) immuno-diagnostic methods which require further study and development. In addition, he points out the need of a fourth method based on inoculation of fecal material from patients into the cecum of rabbits and guinea pigs for detecting light infections by producing amoebic dysentery in them where other methods failed to elucidate the cause of symptoms in the patients.

Amoebae can be cultured "in vitro" successfully by introducing an inoculum of intestinal contents containing them into a diphasic medium. Such cultures contain many species of bacteria and, therefore, are considered as "crude" in contrast to those containing but a single species and designated as monoxenic. Because of the activities of the bacteria, crude cultures are not useful for studies on the metabolism of the amoebae, nor on pathogenicity and chemotherapy in experimental animals. However, they have provided abundant information on the stages of encystation, excystation, and metacystic development but none on the transitional growth from tiny amoebulae to large trophozoites. In addition crude cultures provide a constant and ample supply of cysts for studying the effect of chemical agents on them in potable water, on leafy vegetables, and in other situations.

The complicating factors introduced by bacteria in crude cultures can be eliminated by establishing bacteria-free cultures. The methods are (1) trophozoites from bacteria-free amoebic liver ulcers, (2) freeing cysts from bacteria by chemical treatment, (3) micro-isolation of cysts, and (4) treatment of cultures with antibiotics effective against the bacteria but tolerated by the amoebae. Having obtained bacteria-free amoebae, a single species of bacteria may be introduced to produce monoxenic cultures.

E. histolytica can be grown in monoxenic cultures containing bacteria, especially *Clostridrium perfringens*, or *Trypanosoma cruzi* which produce factors essential to the growth of the amoebae. While excystation of the amoebae occurs in anaerobic bacteria-free cultures containing an enriched balanced salt solution, division does not. *E. histolytica* probably is an anerobe. "In vitro" evidence indicates that it is a phagotroph. Since all attempts to produce it in associate-free cultures have failed, the author visualizes such a project as an attractive problem for a team of investigators, including protozoologists, bacteriologists, physicists, biochemists, and physiologists.

Currently 27 agents, including four preparations of emetine, seven aromatic arsenicals, three iodoquinolines, seven antibiotics, one Kurchi alkaloid, one German product (Gavano), one acridine, two bismuth compounds, and chloroquin, have been used against amoebae. Most "cures" have relapsed when observed continuously over a longer period. Emetine is promising against amoebae in liver abscesses but has serious effects on cardiac muscle. The aromatic arsenicals and iodoquinolines are useful against amoebae in the intestine.

Problems in screening drugs "in vitro" arise from the fact cultures contain other organisms whose products are essential to the survival of the amoebae. Hence a compound appearing to be amoebostatic or amoebicidal may be only bacteriostatic or bactericidal.

Pathogenicity in the intestine appears to be associated with the presence of bacteria. Bactericidal antibiotics relieved severe amoebic dysentery in humans. Virulent strains of amoebae grown in cultures with *Trypanosoma cruzi* failed to produce lesions in bacteria-free guinea pigs when injected into the caecum, whereas animals harboring either *Escherichia coli* or *Aerobacter areogenes* developed lesions. Guinea pigs with normal bacterial fauna readily developed lesions.

Dogs appear to be better experimental animals than kittens, rats, macaques, rabbits, or guinea pigs for testing drugs.

Studies on the fate of amoebicidal drugs in the host as well as on the parasite are prerequisite to comparative tests.

The final chapter by Clarence A. Imboden, M.D., sets forth in concise fashion information on the etiology, intestinal and extraintestinal pathology, management, and treatment of amoebiasis.

The trophozoite is the vegetative form that invades the tissues. Under appropriate conditions, it encysts. Infection occurs upon ingestion of the cyst and liberation of the amoeba.

Large and small races are recognized with the large one being pathogenic. Pathogenicity is associated with the enteric bacterial flora. Diet doubtless influences the flora and therefore the pathogenicity of the amoebae. Individual host resistance or susceptibility likewise play important roles.

The most severe intestinal lesions appear in clinical cases but a surprising amount of pathology occurs with minimal symptomatology. Lesions are most common in the caecum, proximal ascending colon, and sigmoid or rectosigmoid regions.

The initial mucosal lesion in the intestine is a small superficial pinpoint crater with a yellow center and erythematous areola. It develops into a flask-shaped ulcer. The most common intestinal lesion is the "amoeboma," an inflammatory tumor. Massive haemorrhage may occur from erosion of a large vessel or profuse oozing from extensive ulcers.

Extra-intestinal lesions are metastatic from intestinal sites. Liver lesions are most common in the right lobe, probably

due to hemodynamics of portal circulation from the colon. Pulmonary amoebiasis is usually secondary to liver involvement. Brain tumors are rare and practically never encountered except in cases of liver and lung infection. Cutaneous amoebiasis occurs in fistulous openings around the anus.

Clinical manifestations are set forth as (1) chronic intestinal amoebiasis, the most common, (2) acute intestinal amoebiasis (dysentery), (3) intestinal complications, and (4) extra-intestinal complications. Each of these phases is discussed.

All infections of amoeba should be treated. Therapy should encompass intestinal flora as well as the parasite. Treatment should take into consideration intestinal and extra-intestinal infections.

O. Wilford Olsen,
Department of Zoology,
Colorado State University

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PRACTICAL ALLERGY—M. Coleman Harris, M.D., F.A.C.P.; Norman Shure, M.D., M.S., F.A.C.P. F. A. Davis Company, Philadelphia, 1957. 471 pages, $7.50.

This is an excellent treatise on clinical allergy as encountered in medical practice. It is replete with information. The manner of writing is direct, concise, easy and pleasing to read.

The perusal of each chapter and indeed of nearly every paragraph will review available knowledge and stimulate and enlighten any physician who assumes the responsibility of study and control of some or all of the problems which are due primarily or secondarily to allergy. Allergists also will be benefited by reading each chapter. Such review of our present knowledge and experience and technique in diagnosis and treatment of other allergists is most important. It will acquaint them with the ideas of two veteran workers in this field and may yield increased efficiency and improved results in the readers' clinical efforts.

As the book has been carefully read by this reviewer the following chapters seem of special value because of their information and for later references: The Nature of the Allergic Reaction; The History and Physical Examination; Laboratory Procedures; Bacterial, Physical and Insect Allergies; Pollen as a Cause of Allergy—with its carefully compiled lists and frequencies of pollens in many areas throughout the United States; Drug Reactions—in which a list of symptoms from most important allergenic drugs is contained; Collagen Disease—a very concise and helpful chapter; The Emotional Factor—a reasonable and helpful chapter; Office Allergy Technique; Materia Medica—in which all groups of drugs and hormones available for allergy practice are listed.

The important care and sterilization of syringes, needles, vials and the types of extraction and diluting fluids is most important to keep in mind even though a physician is not making his pollen extracts, other inhalant antigens, vaccines and allergens for testing in his own laboratories.

Chapters on the diagnosis and treatment of manifestations of clinical allergy are concise and informative even though space in a treatise of this type did not allow details of histories, methods of study, and results of indicated therapy. Because of the variations in methods of study and control of clinical allergies, no reviewer would agree with all opinions of the authors. This is especially true of the many manifestations, methods of diagnosis and control of food allergy.

This well-written, informative and withal concise book on Practical Allergy should be read, studied and held for ready reference by all physicians and allergists who assume the challenge of aiding and controlling the many manifestations of clinical allergy.

Albert H. Rowe, M.D.

PEDIATRIC ROENTGENOLOGY—Dr. M. A. Lassrich, Prof. Dr. R. Prévot, Prof. Dr. K. H. Schäfer, Hamburg. Edited by Prof. Dr. K. H. Schäfer, Hamburg. Translation from the German provided by James T. Case, M.D., D.M.R.E. (Cambridge), Professor Emeritus, Radiology, Northwestern University Medical School, Chicago; Director, Memorial Cancer Foundation, Santa Barbara. Grune & Stratton, Inc., New York, 1957. 333 pages, 700 illustrations, $28.00.

This well printed and well arranged monograph is divided into three main sections dealing respectively with disorders of the thoracic organs, the abdominal organs, and the skeletal system.

The section on thoracic organs is subdivided into chapters covering the normal thorax, the pathologic thorax, both of these terms applying to the upper and lower respiratory tract, and the heart and great vessels.

The section on abdominal organs is divided into preliminary considerations of abdominal roentgenography, normal and abnormal findings in the alimentary tract, biliary tract, genitourinary tract, and adrenals. The skeletal system deals with normal and abnormal findings in the skull, vertebral column, bones of the thorax, pelvis, extremities and soft tissues.

While the reproductions are in positive form, the detail is so good, and the accompanying diagrams and legends so clear that they must be regarded as outstanding. The material comes from the University Children's Clinic and the Central Radiation Institute of the University of Hamburg. This is the first English translation of the 1955 German edition and was printed in Germany. It is one of the best illustrated monographs on pediatric roentgenology with which this reviewer is acquainted.

L. H. Garland, M.B.

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MANAGEMENT OF COMPLICATIONS IN EYE SURGERY—Edited by R. M. Fasanella, M.D., Chairman, Section of Ophthalmology, Yale University School of Medicine. W. B. Saunders Company, Philadelphia, 1957. 422 pages, illustrated, $16.00.

Most of the textbooks on ophthalmic surgery devote insufficient space to the prevention of the pitfalls and the management of the complications of eye surgery and injuries. It has been said many times that "the only surgeon who does not have complications is one who does not operate." It is therefore refreshing to find a book the entire contents of which deals with these important subjects.

The book consists of 23 chapters which have been contributed by some of the outstanding eye surgeons of this country. These chapters cover the pitfalls and complications of the various surgical procedures currently used in ophthalmology. The editor of the volume has chosen authors of the various chapters because of their particular interest in their subject. For example: Paton on keratoplasty; Berke on ptosis surgery; Pischel on retinal detachment surgery; and Kronfeld on delayed restoration of the anterior chamber after cataract surgery.

Of particular importance are the chapters on Anesthetic Complications by Atkinson; Medical Complications of Eye Surgery by Bondy of the Department of Medicine of Yale; and the Psychiatric Aspects of Ocular Surgery by Lincoff. The final two chapters on Rehabilitation of the Low Vision Patient by Fonda and the Estimation of Loss of Visual Efficiency by Spaeth, Fralick and Hughes add to the value of the book.

The format is good, the reproduction of photographs and line drawings is excellent and the type and paper are up to the usual Saunders' high standard. The index of 13 pages is complete and covers the material adequately.

The book is a must for the ophthalmic surgeon.

Frederick C. Cordes, M.D.

SIGNS AND SYMPTOMS—Applied Pathologic Physiology and Clinical Interpretation—Third Edition—Edited by Cyril Mitchell MacBryde, A.B., M.D., F.A.C.P., Associate Professor of Clinical Medicine, Washington University School of Medicine. J. B. Lippincott Company, Philadelphia, 1957. 973 pages, 191 illustrations, 6 color plates, $12.00.

The editor of this book and the twenty-six other authors who have written the thirty-four respective chapters acquaint the reader with the most common symptoms and findings which cause people to seek the care of a physician. They have followed carefully a plan to develop a quality of analysis which uses a knowledge of physiology as its central structure and to point out essential deviations from the normal which may have a wide variety of causes, including organic disease. Although the obvious objective is toward accuracy and diagnosis, which is based on understanding fundamental processes, it is written, nevertheless, in a concise and interesting manner.

Emphasis is given to the advantages of obtaining a good history as it might be developed by the use of the physiologic approach rather than by following a stereotyped form. The editor's introduction, which discusses the process of analyzing and interpreting symptoms and findings, is an excellent statement and contains advice from which every practicing physician and every medical student can profit. At the conclusion of each chapter is a comprehensive list of references to original articles from which one could expand his reading and, thereby, his knowledge of particular symptoms and findings.

The book is a scholarly and informative presentation of important practical topics. It is well illustrated by prints of pertinent diagrams, charts, and photographs (some in color) which clarify respective texts. It is recommended as a book which physicians, medical students, and teachers in medical schools should have available for their personal use, which, no doubt, would be frequent.

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THE FUNCTION OF THE URETER AND RENAL PELVIS—Pressure Recordings and Radiographic Studies of the Normal and Diseased Upper Urinary Tract of Man—Fredrik Kiil, M.D., Research Associate, Institute for Experimental Medical Research, University of Oslo. W. B. Saunders Company, Philadelphia, 1957. 205 pages, illustrated, $7.50.

This interesting monograph of some 200 pages is an important contribution to the numerous studies that have been made on the activity of the human ureter under various normal and pathological conditions. It is primarily a research study, with only a relatively minor effort to apply the findings and conclusions to clinical problems.

The first section of the book is a discussion of methods used both by the author and by previous investigators. The latter are first discussed and their results and conclusions subjected to critical analysis. These studies have been done, of course, both on isolated ureteral preparations and on living human patients. His opinion is that the latter are the only reliable methods, and he describes in some detail the equipment and technique he employs, which is essentially a graphic manometric recording of the ureteral pressure and activity synchronized with pyeloureterograms obtained by the simultaneous use of two small catheters in the same ureter. He is convinced that there is no evidence that ureteral activity is influenced by mechanical irritation from the catheters.

The second section of the book concerns his findings with various conditions and stimuli affecting the normal ureter, emphasizing the effect upon the normal intraureteral pressure and the height and frequency of contractions. He has definite opinions on several controversial questions. He finds no evidence of any kind of nervous control of ureteral activity; he states that bladder distention causes no effect on ureteral contractions until the bladder pressure exceeds the pressure in the lower ureter; he finds no evidence for any kind of specialized closing mechanism at the ureterovesical junction, and believes that normally reflux is prevented only by the obliquity of the channel through the bladder wall.

Experiments were made with many of the drugs alleged to affect ureteral activity and none of them were found to have any significant influence upon tone or contractions. The absence of such effects from several anticholinergic drugs confirms his opinion that the ureter, unlike the gastrointestinal tract, is not under the control of the parasympathetic nervous system.

The final section discusses briefly ureteral activity in several types of clinicopathological conditions, especially various types of hydronephrosis, including that of pregnancy, which he conceives to be entirely a mechanical obstruction; the effect of prostatism, and there is included a brief consideration of the possible causes of megaloureter.

The author is not dogmatic in his conclusions. He merely reports factually his findings and the interpretations and conclusions he feels may properly be drawn. He describes with equal honesty the points in which he fails to agree with former studies and where he confirms the findings, pointing out the limitations of the work and the possible sources of error. It will be a valuable book for the scientifically inclined, not only for the information it gives, but as a basis for some individual thinking.

LYLE G. CRAIG, M.D.

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EXTENSILE EXPOSURE—Second Edition—Arnold K. Henry, M.B., Dublin; M.Ch. (Hon.) Trinity College, Dublin and Cairo. The Williams and Wilkins Company, Baltimore, 1957. 320 pages, $10.00.

The title of this book, when understood, explains its purpose. Exposure during surgical operations must have a range adequate to permit the surgeon to accomplish his work with maximal ease and minimal trauma. This range of surgical exposure is necessarily expansile and extensile, hence the title "Extensile Exposure." The author is an Emeritus Professor of Clinical Surgery in the University of Egypt and a Professor of Anatomy in the Royal College of Surgeons of Ireland. The combination denotes an interest and experience which should result in a practical sound work which would be specifically designed for the operating surgeon. This, in fact, has been admirably accomplished, and attests the need for continued revisions and editions of this book as surgery progresses.

Extensile Exposure concerns itself primarily with the exposure of the extremities. However, the neck, the costal arches, and the hypogastric exposures as related to exposure of the extremity structures are included. The illustrations are excellent, and the style is practical. The exposures described and illustrated are direct, anatomical, and well conceived. It is on the whole an excellent book on extremity exposures.

The only objection which the reviewer finds in the book is its rather ponderous style in numerous interspersed sentences which abound in metaphors and similes. At times the author strives more for elegance of expression than clarity, and does not follow the introductory maxim of Anatole France . . . d'abord la clarté, puis encore la clarté, et enfin la clarté. These passages make for uneven reading of the main portion of the text which is direct and clear. The book will be welcome reading to the surgeon who wishes good concise discussion and illustration of the surgical anatomy of the extremities.

VICTOR RICHARDS, M.D.

THE RIDDLE OF STUTTERING—C. S. Bluemel, M.D., The Interstate Publishing Company, Jackson & Van Buren, Danville, Illinois, 1957. 142 pages, hard bound, $3.50; paper bound, $1.50, accompanying 4 therapy records, $3.00.

This book—according to the author—presents his conclusions for the appraisal of the speech correctionist and the stutterer himself. This task is as courageous as it is dangerous. The speech correctionist lacks psychiatric training and lacks therefore the necessary experience in diagnosis and treatment of neurosis. The patient himself will try to find in this book his own emotional story and might identify himself with somebody else's problem instead of finding himself—without a book, but through psychotherapy. To make things more complicated, the author tries to find new meaning in the semantic difference between stuttering and stammering. While the medical speech specialist tries to simplify the situation by eliminating the term "stammering" and by calling the whole syndrome "stuttering," the author proposes to call nonorganized speech, prespeech or speech in the making "stuttering" which can be carried into adult life as subnormal speech function. Nonorganized speech is differentiated from disorganized speech, marked by blocking and called "stammering." While stuttering is considered a developmental deficiency of speech, stammering is called a neurotic disorganization. To the reviewer these theories come close to playing with words and one feels reminded of Mephistopheles in Goethe's Faust: "When ideas fail, words come in very handy."

Besides most interesting observations on personality traits of stutterers one finds the wrong statement that stammering seems to be especially common among Germans, a fact which he blames on the mechanical difficulty of the language "for the consonants come in chunks," while there were less stammering in Spain and Italy partly because of the culture in which the language is employed and partly because of the nature of the language. The author forgets the rareness of stuttering in the Chinese and the American Indians which has nothing to do with language but with the child's security within the family.

The author hopes that neuropsychiatry may offer yet help for the problem of stammering and stuttering, although he thinks that Freudian theories seem to be exhausted. He therefore assumes that Freudian theories are static and have reached a dead end! The bibliography is part of a chapter "Retrospect" and does not represent an informative source of historical information. The therapeutic outline is as incomplete. Even the chewing method by Froeschels is not mentioned. Still the ideas of the author are worthwhile for the physician interested in the personality traits of the stutterer.

PAUL J. MOSES, M.D.

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THE YEAR BOOK OF OBSTETRICS AND GYNECOLOGY—1957-1958 Series—Edited by J. P. Greenhill, B.S., M.D., F.A.C.S. The Year Book Publishers, Inc., 200 East Illinois Street, Chicago, 1957. 597 pages, $7.50.

This is the annual compilation of abstracts from the significant literature in this field, edited under the direction of Chicago gynecologist and obstetrician, J. P. Greenhill. The articles abstracted are taken from journals received between July 1956 and July 1957. The material is evenly divided between obstetrical subjects and gynecological ones.

In obstetrics, adequate attention is given to the timely subjects of postmaturity, coagulation defects, and perinatal mortality. Practically all the authoritative literature on these matters is covered. In gynecology, forty-six pages and some thirty articles are devoted to infertility, a not disproportionate ratio. Under operative gynecology, the majority of articles are concerned with urinary relationships (particularly stress incontinence), demonstrating the increasing attention being given to gynecologic urology in this field. The discussion of malignant tumors occupies approximately one-fourth of the section on gynecology.

A special feature of this edition is an article "Genetic Considerations in the Practice of Ovarian Irradiation for the Treatment of Sterility" by L. B. Russell of the Biology Division, Oak Ridge National Laboratory. This short article discusses in general terms some of the genetic aspects of this subject and is recommended reading. It carries a short bibliography.

As usual, the editor's comments add much to this book. He surveys additional pertinent literature not covered by the abstracts. His comments in this edition reflect an increasing awareness of medico-legal implications affecting the specialty.

This book can be recommended to any practitioner working in this field and wishing a handy reference of abstracts of current literature.

KEITH P. RUSSELL, M.D.

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THE PATHOLOGY AND SURGERY OF THE VEINS OF THE LOWER LIMB—Harold Dodd, Ch.M. (Liverpool), F.R.C.S. (Eng.), Surgeon to St. Mary's Hospital (London) Group; and Frank B. Cockett, M.S. (London), F.R.C.S. (Eng.), Surgeon to St. Thomas's Hospital, London. E. & S. Livingstone Ltd., Edinburgh and London, 1956. Distributed in U.S.A. by Williams and Wilkins Company, Baltimore, 1956. 462 pages, $12.50.

This book is written in a concise and clear manner, and covers admirably the subject of venous disorders of the lower leg. The approach is stimulating and interesting. The experience of the author is rich and well presented. The surgical anatomy of the veins of the leg is presented in a graphic and succinct manner. The pathological physiology of venous disorders of the limb is well discussed. The treatment of varicose veins, varicose ulcers, and phlebitis as recommended by the authors is sound and rewarding. The book can be recommended to anyone interested in a deeper understanding of venous disorders of the lower limb.

VICTOR RICHARDS, M.D.

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SPEECH CORRECTION AT HOME—Morris Val Jones, Ph.D., Director, Speech and Reading Clinic, Morrison Center for Rehabilitation. Charles C. Thomas, Publisher, Springfield, Illinois, 1957. 138 pages, $4.75.

This book intended for the family of speech-handicapped individuals is of practical value for physicians who want to place useful material in the hands of the mother of a speech-defective child or the wife of the aphasia patient. It contains a good description of normal and faulty speech development, it describes helpful hints for the improvement of the emotional situation of the stutterer. Exercises for children with cleft palate, open bite, cerebral palsy are given. The laryngectomized patient finds directions for the "do-it-yourself" training of esophageal voice.

The special value of this book is in the encouragement of the family and the patient, but also of the physician that speech therapy is by no means a mystic and magic field which is reserved for members of the guild of a few—certainly nonmedical—specialists. Speech defects need daily care at home since correction in school cannot be given often enough due to the enormous case load. The necessary exercises are described in simple form. Psychological theories are omitted. The bibliography—as we find it so often in books by speech therapists—does not contain any material written by physicians.

PAUL J. MOSES, M.D.

APPLICATION FOR HOUSING ACCOMMODATIONS

FOR YOUR CONVENIENCE in making hotel reservations for the coming meeting of the **California Medical Association,** April 27 to 30, 1958, Los Angeles, hotels and their rates are at the right. Use the form at the bottom of this page, indicating your first and second choice. Because of the limited number of single rooms available, you will stand a much better chance of securing accommodations of your choice if your request calls for rooms to be occupied by two or more persons. **All requests for reservations must give definite date and hour of arrival as well as definite date and approximate hour of departure; also names and addresses of all occupants of hotel rooms must be included.**

ALL RESERVATIONS MUST BE RECEIVED BEFORE: APRIL 1, 1958

Eighty-seventh Annual Session
CALIFORNIA MEDICAL ASSOCIATION
Los Angeles, California
APRIL 27-30, 1958

HOTEL ROOM RATES *

	Single	Twin Beds	Suites
AMBASSADOR HOTEL			
3400 Wilshire Boulevard			
Main Building	9.00-19.00	12.00-22.00	28.00-38.00
Garden Studios	17.00-23.00	22.00-30.00	40.00-54.00
CHAPMAN PARK HOTEL			
3405 Wilshire Boulevard		12.00-16.00	20.00-25.00
THE GAYLORD HOTEL			
3355 Wilshire Boulevard	8.00	10.50	18.00
HOTEL CHANCELLOR			
3191 West Seventh Street	7.00- 8.00	10.00-12.00	
SHERATON-TOWN HOUSE			
2961 Wilshire Boulevard	11.00-18.00	16.00-23.00	31.00

*The above quoted rates are existing rates but are subject to any change which may be made in the future.

CALIFORNIA MEDICAL ASSOCIATION
450 Sutter Street—Room 2000
San Francisco 8, California

Please reserve the following accommodations for the 87th Annual Session of the California Medical Association, in Los Angeles April 27 to 30, 1958.

Single Room $..... Twin Bedded Room $.....

Small Suite $..... Large Suite $..... Other Type of Room $.....

First Choice Hotel..... Second Choice Hotel.....

ARRIVING AT HOTEL (date)..... Hour:.....A.M.....P.M. } Hotel reservations will be held until

Leaving (date)..... Hour:.....A.M.....P.M. } 6:00 P.M., unless otherwise notified

THE NAME OF EACH HOTEL GUEST MUST BE LISTED. Therefore, please include the names of both persons for each twin-bedded room requested. Names and addresses of all persons for whom you are requesting reservations and who will occupy the rooms asked for:

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Individual Requesting Reservations—Please print or type Delegate?..... Alternate?.....

Name..... County.....

Address..... City and State.....

CANCER COMMISSION
CALIFORNIA MEDICAL ASSOCIATION

PRE-CONVENTION CONFERENCES

LOS ANGELES • SATURDAY, APRIL 26

Radiology

West Venetian Room, Ambassador Hotel

Chairman . . . . . Eugene G. Tainter, M.D., Sacramento

Secretary . . . . . Louis Bonann, M.D., Los Angeles

DIAGNOSTIC SESSION—9:30 a.m. to noon

Twelve diagnostic cases with histories and films will be presented. Cases have been selected to illustrate specific problems in the radiological and clinical diagnosis of cancer. Audience participation and discussion are urgently requested.

THERAPY SESSION—2:00 p.m. to 4:30 p.m.

Five cases with specific therapy problems will be presented. The audience is asked to participate actively.

Pathology

9:15 a.m. to noon • 2:00 p.m. to 4:30 p.m.

East Venetian Room, Ambassador Hotel

Moderator: PAUL MICHAEL, M.D., Oakland

The Pre-Convention Conference on the Tumors of Childhood will be conducted under the chairmanship of George J. Hummer, M.D., Santa Monica.

Members who wish to attend this conference are requested to register now with Weldon K. Bullock, M.D., Registrar, Tumor Tissue Registry, C.M.A. Cancer Commission, Los Angeles County Hospital, 1200 North State Street, Los Angeles 33.

7:00 p.m.

Dinner meeting of the California Society of Pathologists. For reservations contact Ernest Simard, M.D., Secretary, 708 Cass Street, Monterey.

Cancer Commission Dinner

6:30 p.m.—Frenchette Room

Annual Dinner Meeting of the Cancer Commission and Advisory Committee.